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VOLKMANN'S ISCHEMIC CONTRACTURE*

An Analysis of Its Proximate Mechanism

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BOSTON

SINCE 1871, when von Volkmann first described the contracture deformity that bears his name, it has commonly been accepted as a complication of the improperly treated supracondylar fracture of the humerus. This paper presents evidence that Volkmann's ischemic contracture has no essential connection with such a fracture or any other specific injury but is the result of ischemic infarction produced by segmentary arterial spasm of the main artery to an extremity, with reflex spasm of the collateral circulation. Thus, a subtotal ischemia is produced, and the muscle bellies, which have the greatest demand for arterial blood and are therefore the most vulnerable tissue to its loss, are the first affected. Gangrene of the fingertips or partial or even complete gangrene of the extremity would result if this spasm continued in sufficiently severe degree, but where Volkmann's contracture is to be the only result, some improvement in the arterial supply intervenes. This vasomotor activity is under control of the sympathetic nervous system, and will be discussed more fully after the actual clinical picture has been considered.

The problem can be further defined by the statement that only the acute stage of Volkmann's contracture is concerned in this study. Whatever one may believe to be the responsible factors, the lesion initially is one of impaired circulation. In the old cases of established deformity, normal blood supply has returned, and the problem is entirely one of correcting existing deformity by physiotherapy, tendon lengthening, bone shortening and so forth. These procedures have been discussed elsewhere, and are not considered in this paper, which is limited to a discussion of Volkmann's contracture in its acute stage, the actual mechanism producing the ischemia and the logical methods of correcting the causative lesion; the goal of treatment is to restore adequate circulation before irreparable damage is done, and thus to avert contracture deformities.

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RECENT CLINICAL EXPERIENCE

In the literature of the last five years, most particularly in the last two years, from France, England, Switzerland and occasionally from South America, numerous articles, mostly from unrelated sources, have described the operative findings in explored cases of early Volkmann's syndrome. Thirty of these case histories were reviewed, and findings of the various operators were strikingly similar. The antecedent injury was usually a fracture or bullet wound of the upper arm. In about twenty-four hours, definite signs of ischemia appeared: the hand became cold and swollen, with usually a pale cyanosis, and the fingers became functionless. Pain was a prominent symptom, especially on any attempt at motion of the fingers, either active or passive. The radial pulse was absent. If the condition was further observed, the next day the fingers usually assumed a position of flexion, and any attempt to straighten them caused considerable pain. When apparatus was used to maintain extension of the fingers, the patient could not tolerate it for long, even with repeated doses of morphine, and it invariably had to be removed. In these cases, the surgeon, after intervals varying from twenty-four hours to three weeks, finally decided to explore the injured site. It is interesting that in most cases the surgeon had not explored such an injury before and was not prepared for what he found. He went in expecting to find some mechanical obstruction to the arterial flow, angulation of the artery over the

proximal fragment or pressure of fragments on the artery, hematoma or some other mechanical disturbance that he hoped to be able to correct; accordingly, these men could certainly not be accused of the possible inclination of an enthusiast to read into his findings something that he was looking for. This, I think, gives added weight to the observation that in every case a profound segmentary arterial spasm was encountered. The operative note might have been as follows:

> A longitudinal incision was made medial to the biceps tendon, and in the lower half of the incision, no bleeding occurred. The muscle, which herniated through the superficial fascia when it was incised, appeared gray and lifeless. There was some extravasated old blood, but no hematoma under pressure. The median nerve was not remarkable. The brachial artery, however, presented a most astounding picture. At a point about 2 cm. above its bifurcation, it was pulsating normally, was even perhaps a little dilated, but there it suddenly became narrowed to a stringlike size extending down into the radial and ulnar branches.

The foregoing description is not taken from any one case but is a synthesis of so many reports that it is almost universally applicable. The methods by which these surgeons attempted to treat the patients are discussed below. The important point is that in patients presenting definite signs of an early Volkmann's syndrome with an absent radial pulse, a cold pallid ischemia and a beginning flexion deformity of the fingers, exploration generally revealed a segmentary spasm of the main artery. Although arterial spasm of varying degrees has been recognized in many peripheral vascular disorders, it has not until very recently been suspected of being responsible for such severe ischemia, and this series of cases establishes arterial spasm as a phenomenon to be reckoned with.

Pathology

As a background for this discussion of how the established Volkmann's contracture is produced by this mechanism, a review of its pathology is necessary. It is essentially an atrophy of the flexor muscle bellies, whose destruction results in an apparent shortening of the flexor tendons, pulling the fingers and sometimes the wrist into acute flexion (Fig. 1). In the less severe cases, by flexion of the wrist, the fingers can be extended and vice versa, but extension of both fingers and wrist is not possible at the same time. In the severer cases, neither can be done.

One of Griffiths's[1] contributions to this subject is his very precise description of the morbid anatomy. The gross picture, which is one of central degeneration of the muscle bundle, is duplicated histologically by only one other condition, infarction. In both, there is a picture of mass necrosis; the most extensive degeneration occurs in the center of the muscle sequestrum, and cellular activity and fibrosis take place only at the periphery, which is surrounded by a sheath of dense fibrous tissue. In the center of the mass, the muscle fibers lose their nuclei and cross striations, and fuse into a homogeneous mass, little more than a defining membrane separating them (Fig. 2). As the periphery is approached, some

Figure 1. *Clinical Deformity in a Case That Was Not Severe to Begin with and That Was Further Improved by Operative Lengthening of the Flexor Tendons.*

Note the atrophy of the forearm. With the wrist flexed, the fingers could be fully extended, and with the fingers flexed, the wrist could be fully extended, but both could not be done at once.

signs of function are preserved, and there is an area of intense cellular activity, both fibroblastic and phagocytic (Fig. 3). This picture is in contrast to muscle degeneration from all other causes, such as denervation and sepsis, when the appearance is one of diffuse interfibrillar fibrosis (Fig. 4). This histology should be kept in mind when one considers the mechanism of the

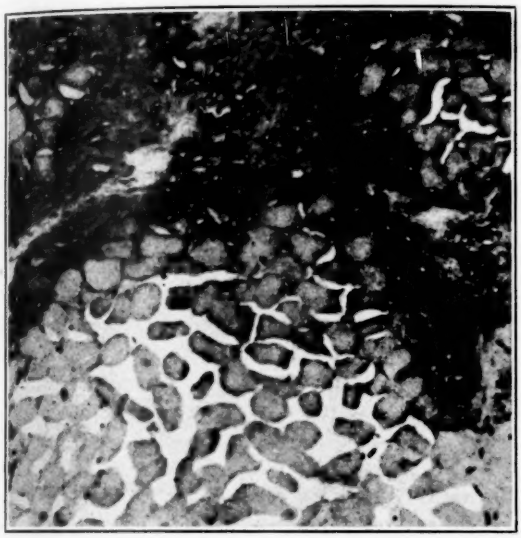

FIGURE 2. *Low-Power View of a Cross Section of the Flexor Muscles of the Forearm in a Case of Volkmann's Contracture.*

Note the mass necrosis of the muscle bundles, with the greatest destruction in the center and with the cellular activity limited to the periphery (Griffiths[1]: reproduced with permission of the publisher).

ischemia. It is also of value in animal experimental work in determining whether or not a true Volkmann's contracture has been produced.

ETIOLOGY

The fact that supracondylar fracture of the humerus is the commonest initial injury that Volkmann's contracture may complicate has perhaps led many to associate the contracture exclusively with such fractures. The location of this fracture and the related displacement that commonly occurs unquestionably bring into play many factors tending to impair circulation of the forearm. Among these are the possible angulation of the brachial artery over the edge of the proximal fragment, the damage to soft tissue from spicules of bone and, most commonly mentioned, the possibility of hemorrhage into the antecubital fossa, with the formation of a hematoma confined by the unyielding deep fascia and thereby tamponading the venous return. It has been pointed out that such a pressure hematoma is especially effective at this point because the venous return from the forearm converges into a plexus that is particularly vulnerable to local pressure. If to this is added a difficult and unskillful reduction, and the application of some constricting apparatus in a position of acute flexion, the *coup de grâce* may be administered to the circulation of the forearm.

That this is a reasonable and adequate picture of circulatory embarrassment cannct be denied and, in fact, very logically explains its almost unchallenged acceptance for so long. And I have no desire to suggest that these factors are not important. It is obvious that in any situation in which ischemia is present, any factor that impairs circulation in any way must never be tolerated. No doubt, it is possible to shut off the circulation to any extremity by overly tight splints, and perhaps on occasions this has been done. It is self-evident that prompt, gentle and skillful reduction, and properly applied fixation are fundamental

FIGURE 3. *High-Power View of the Specimen in Figure 2.*

Note that the muscle fibers near the periphery retain their cross striations and are more nearly normal (Griffiths[1]: reproduced with permission of the publisher).

essentials. Given these, this syndrome has developed right under the eyes of the most capable surgeons; even when they had the opportunity of treating the patient from the beginning.

The chief evidence that the factors of venous occlusion and constriction of overly tight apparatus do not constitute the essential mechanism of Volkmann's ischemia is that actually the syndrome commonly develops in the complete absence of such causes. In cases of supracondylar fracture in which these factors might reasonably be expected and in which the fracture site has been

exposed by open operation, the subfascial hematoma as such has rarely been found. There is a certain amount of old blood clot and loose hemorrhage in the tissues as at any fracture site, but no specifically confined mass. The most approved treatment has consisted in multiple drainage incisions through the fascia; but this procedure, in addition to the removal of all apparatus, has in many cases not improved the circulation, and when improvement occurs, the artery itself has usually been exposed and freed. I consequently believe

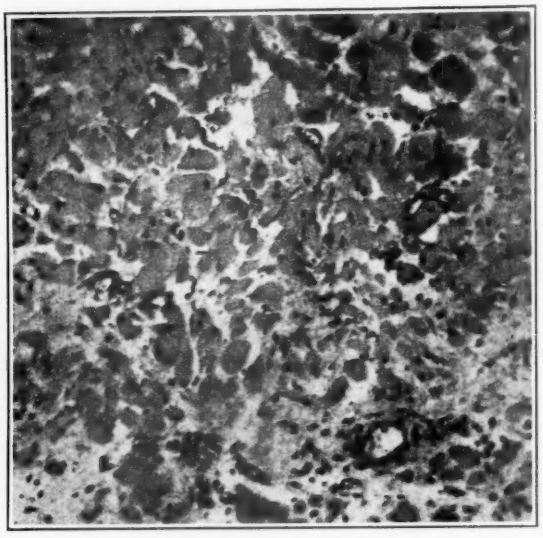

FIGURE 4. *Cross Section Showing the Histologic Picture of the Muscle Atrophy from All Other Causes.*

Note the diffuse interfibrillar fibrosis, as contrasted with the picture in Figures 2 and 3. This difference seems to be the best argument against the theory of venous occlusion, since one would expect the above picture if Volkmann's contracture was the result of venous occlusion, with edema and retention of metabolic waste products (Griffiths[1]: reproduced with permission of the publisher).

that the procedure has fortuitously achieved the result of releasing reflex arterial spasm.

Further evidence against these factors is that this particular injury, which most favors their presence, is by no means the only one that Volkmann's ischemia may follow. It occurs in practically all fractures of the upper extremity, even those as far removed as the clavicle, in several other injuries to soft parts in which no fracture has occurred, and in similar injuries of the lower extremities. Hill and Brooks,[2] in 1936, reviewed the literature and found 123 cases without the previous application of any constricting bandage or splint, and 28 cases in which there was neither any fracture nor constricting bandage or splint. Furthermore, many cases of soft-tissue injury with only moderately severe trauma are described, and Griffiths[1] reports 3 cases following arterial embolism from heart disease in which there was no trauma of any kind.

These facts may afford some comfort to the surgeon who has seen this complication develop in a patient under his care. They suggest that the proximate mechanism is initiated by the injury itself rather than by the treatment, and that it is an ischemia intrinsically arterial in which other factors are only secondary.

Arterial Spasm

Leriche[3] has written a great deal on circulatory equilibrium, which is ensured for each structure by the action of the vasomotor nerves. These nerves adapt the local circulation to the regional requirements by vasoconstriction or vasodilatation as a result of constantly changing stimuli. Leriche differs from many physiologists in his opinion that the sympathetic system contains sensory as well as motor fibers and that the sympathetic ganglion plays the role of reflex center. It is easy to believe, therefore, that the sympathetic system may have a definite role to play in injury by which a local temporary arterial spasm may be set up to prevent overextravasation of blood or fatal hemorrhage from a severed artery. If these stimuli are not removed, or if the patient has an especially labile vasomotor reflex, the spasm may persist beyond its physiologic requirements and may even spread to include the collateral circulation.

Varying degrees of arterial spasm are encountered in many peripheral vascular disturbances. Homans's[4] book on circulatory diseases of the extremities contains a whole chapter on this subject. There is, no doubt, a difference in the mechanism of production between a generalized vasoconstriction and local segmentary spasm; the former is probably due to central innervation and the latter is possibly the result of a local reflex. This point was brought out by Homans[5] in discussing a case of his in which an adequate and satisfactory ganglion injection failed to relieve a local arterial spasm; about twenty-four hours later, the foot became suddenly flushed with an extensive vasodilatation. He logically concluded that local spasm may be effected by a distal reflex arc that does not include the ganglion. Injury need not directly affect the vessel to produce arterial spasm. The following case illustrates this fact.

CASE 1. A young, muscular, colored man was admitted to the Boston City Hospital immediately after an altercation with some "friends." The admission diagnosis was bullet wounds of the chest and of the right upper arm and surgical shock. I happened to be in the hospital at the time, and I went to see the man immediately, being concerned particularly about the shock aspect of the diagnosis. To my surprise, I found him reclining on one elbow,

chewing gum, and grinning with considerable self-satisfaction. Obviously, he was not in any surgical shock. I picked up his wrist to feel his pulse, but there was none. The house officer who had admitted him had apparently made the same finding, which accounted for the shock diagnosis, but had neglected to feel the opposite arm, where the patient had a perfectly good full pulse and a systolic blood pressure of 140. Examination of the chest revealed that the bullet wound was superficial, and there were no signs of damage to the lungs; the problem boiled down immediately to the wound of the right upper arm, where there were bullet wounds of entrance and exit through the fleshy portion of the biceps. There was some swelling of this area, but the arm was not grossly distended or tense, and x-ray examination revealed no fracture of the humerus. We believed that some damage had probably been done to the brachial artery, and immediately explored it. Going through the muscle, we found a certain amount of extravasation of blood but no gross hematoma, at least, no hematoma under pressure sufficient to occlude the artery. On exposing the artery itself, we were surprised to find that at a point about 2 cm. above its bifurcation, it was constricted to a stringlike structure. We picked it up and freed it, and followed it along down with the idea of seeing how far this constriction continued, when all of a sudden it began to pulsate and filled with blood. A bystander who was asked to palpate the radial pulse reported that there was good pulse at the wrist. We simply closed the wound, and the patient made an uneventful recovery and never subsequently had any circulatory disturbance in this extremity.

This patient had no direct trauma to the artery, nor was there sufficient extrinsic pressure to occlude it mechanically. He did not, at least at the time of operation, have the essential elements of a Volkmann's contracture because there was still good collateral circulation. Left alone, he might either have spontaneously relaxed the local spasm or later developed reflex collateral spasm. I should probably treat a similar case by ganglion injection, followed by surgical intervention only if collateral circulation became impaired.

Sometimes, segmentary spasm is produced by minor injury to the arterial wall that is not sufficient to occlude the artery by the damage per se but causes the artery to occlude itself. Griffiths[1] describes a patient who was pulseless after satisfactory reduction of a supracondylar fracture. He explored and found no subfascial hematoma, but did find a hematoma no larger than a millet seed in the anterior wall of the brachial artery near the site of fracture. Despite the small size of this hematoma, the brachial artery and its radial and ulnar branches were collapsed and pulseless. Mobilizing and stripping the brachial artery produced no change, but after resection of the damaged portion, the circulation made a complete recovery and no deformity resulted. Griffiths also mentions a case in which the brachial artery showed a very localized intramural rupture, which presented complete spasm from the subclavian artery downward. Several cases are presented in the literature in which resected sections of artery showed, on pathological study, small defects not grossly visible.

Montgomery and Ireland[6] encountered localized arterial spasm in 2 cases, and were stimulated to search the literature for others; in 1935, they reported 44 cases of what they termed "traumatic segmentary arterial spasm," resulting from all kinds of trauma, but of which 26 were the result of gunshot or high-explosive injuries. In 1940, Gage and Ochsner[7] published an excellent report in which arterial spasm is discussed quite fully. They were dealing with the subject of operative procedures on peripheral arteries. They mentioned particularly a so-called "butcher's injury," which results from slipping of the knife during the skinning of beef; a stab wound of the upper medial aspect of the thigh commonly results with injury of the femoral vessels or perivascular tissue in the upper end of Hunter's canal. They noted that in many cases, even when the vessels were not severed, reflex vasospasm was of such severity that the clinical manifestations were identical with those of complete arterial occlusion.

Arterial spasm is also seen following lodgment of emboli, and in fact may result from any disturbance of the peripheral circulation. Homans[4] states that it is known to occur with venous thrombosis, especially the inflammatory sort. One writer[8] graphically referred to this spasm as "arterial colic."

Collateral Circulation

Griffiths's[1] Hunterian Lecture on Volkmann's contracture is the most modern complete discussion of this subject in the literature, and deserves the careful study of everyone interested in the subject. Of the many contributions he makes, I think that the most important is his demonstration by animal experiments that the key factor in the development of Volkmann's contracture is the loss of the collateral circulation. The danger to the peripheral tissues of a main artery in spasm is not so much the loss of the artery itself as a blood-carrying channel as it is the possibility that this spasm may spread to include the collateral circulation as well. Normally, with the main vessels intact, the collateral circulation functions only to a small percentage of its full potential, but its presence affords an alternate route that can, if necessary, be developed to furnish adequate circulation in lieu of the main artery. There are certain anatomic weak points in this system; namely, the common femoral artery, the carotid artery at its bifurcation and the popliteal arteries, about which collateral circulation is not abundant; the regions about the shoulder, elbow, hip, hand

and foot, however, are abundantly supplied. When occlusion of the main artery is a gradual process, simultaneous hypertrophy of the collaterals occurs, and no embarrassment of circulation results. The strain is much greater on the collaterals when the occlusion of the main artery is sudden, and circulation is further imperiled by the fact that the collaterals are subject to the same sympathetic control as the main vessel. Thus, a vicious circle is possible in that if spasm of the main artery becomes fixed beyond its normal physiologic intentions, the same condition may spread to the collaterals at a time when their increased function is needed. It has been shown by oscillometer readings that, with a main artery occluded, reflex vasospasm not only may obstruct the collateral circulation of that extremity but also may affect the opposite side, and even extend to the lower extremity. Thus, without extrinsic pressure, a total or subtotal ischemia may be produced that will result only in muscle atrophy if the ischemia is relatively temporary, and in varying degrees of gangrene if the ischemia is prolonged.

Leriche et al.,[9] working with dogs, were able to resect all the large arteries of the hind legs, beginning distally and operating in eight or nine successive stages spaced at intervals of from ten to thirty days. In this manner, they removed the posterior tibial, the anterior tibial, the femoral, the inferior gluteal, the lateral sacral, the hypogastric, the external iliac and, in the final stage, the common iliac arteries and the bifurcation of the aorta. Carrying out this procedure, they encountered only occasional temporary edema, which rapidly disappeared. These dogs, literally "without arteries," were able to run, stand on hind legs, and jump as normal animals. When the authors attempted initially to resect the common iliac arteries and the bifurcation of the aorta, all the animals promptly died, but if this procedure was preceded by resection of the lumbar sympathetic ganglions, the animals were only slightly disturbed by this extensive arterectomy.

Gage and Ochsner[7] discovered the value of developing the collateral circulation by ganglion block prior to operative procedures on peripheral arteries.

It is evident that good collateral circulation is capable of amply supplying all the needs of the peripheral tissues, and that the chief danger in cases of main-artery occlusion lies in the degree of constriction or dilatation of the collaterals that are under sympathetic vasomotor control. Griffiths, in his animal experiments, showed this loss of the collateral circulation to be the determining factor in the development of Volkmann's contracture.

Treatment

It should be emphasized that time is a major factor in treatment. This syndrome is a progressive one in which more and more damage is done. The value of early action is apparent. In the first place, all measures favoring circulation generally are of fundamental value. These include elevation of the part, removal of any apparatus or circular bandaging, and the application of mild external warmth.

The next logical step is the interruption of the sympathetic reflex arc. Theoretically, one might expect to accomplish this by ganglion injection, periarterial sympathectomy or arterectomy. Ganglion block, which is the simplest of these methods, should be tried first. Its results will be apparent at once, and if the procedure is successful, an open operation is avoided. The following case illustrates its use.

Case 2. A 53-year-old woman was admitted to the Boston City Hospital on September 1, 1941, with a trimalleolar fracture of the left ankle. A Kirschner wire was inserted for traction, and open reduction was later performed under an Esmarch bandage. The operation lasted an hour and a half. The next day, the foot was cold, cyanotic, swollen and painful. The dorsalis pedis and popliteal arteries were not palpable. A lumbar block was done that afternoon. Forty cubic centimeters of novocain was injected, about 15 cc. through each of three needles, and 15 minutes after this procedure, the circulation improved. The following day, both the dorsalis pedis and the popliteal arteries were palpable; 1 week later, swelling of the toes was entirely gone, the foot was warm and pink, the wounds were clean, and the chart was flat. The patient had no subsequent circulatory difficulty.

Lumbar block is now a common procedure when peripheral dilatation is desired, and needs no further comment. Injection of the stellate ganglion is perhaps not so familiar, but reports of surgeons in the French army indicate that it is now being frequently employed in the relief of peripheral spasm of the upper extremity. Luzuy,[10] who apparently was called on to attend a large number of fresh injuries, states that he has had occasion to employ this procedure as often as several times a day. The appearance of the Bernard–Horner syndrome within a few minutes is evidence of successful cervical sympathetic paralysis.

The possibility that local arterial spasm may be the result of a local reflex that does not include the paravertebral ganglions means that this procedure cannot be expected to be universally successful; if circulatory improvement is not promptly apparent, or if initial improvement is not maintained, the artery should be exposed. The adherents to the theory of venous occlusion have logically treated this syndrome by multiple inci-

sions through the deep fascia to afford drainage and relieve pressure. This procedure has been successful in cases in which venous congestion was the main secondary factor, producing the arterial spasm that was the proximate cause of the ischemia. It has failed in many cases when other factors were in effect. I believe that it is therefore more logical to approach the problem directly — to expose the artery by careful dissection. This at once accomplishes effective relief of any abnormal venous pressure, determines whether any local trauma to the artery has been sustained, and affords opportunity for complete sympathetic-arc interruption by periarterial sympathectomy or arterectomy.

Concerning the respective values of these two procedures, there is some difference of opinion among those surgeons who have had some experience in their use. In the series of 30 cases mentioned above, arterectomy was performed in 10, periarterial sympathectomy in 5, and various procedures in the rest — including freeing up of the artery, novocain injection, ligation and simple loose closure. The arterectomy group invariably gave the best results. Definite improvement of circulation resulted in every case, and complete return of normal circulation and function in most cases. In only 1 case[11] did a poor result occur; this patient was said to have had paralysis of the radial, median and ulnar nerves as well, so that the case could hardly be included in a series of pure Volkmann's contractures.

Arterectomy may appear to be a radical procedure,* and a natural reaction is to try to save the artery and hope to re-establish function of this blood-carrying channel. Objections to this are that the alternative periarterial sympathectomy on an extremely contracted artery may be technically difficult, and that interruption of the sympathetic control is the main goal in view. Arterectomy has the advantage of complete interruption of the reflex, in addition to the removal of a segment of artery that possibly contains a small break or tear, not grossly visible, but sufficient to maintain continued abnormal sensory stimuli. Arteriographic studies in late cases of Volkmann's contracture have shown a persistently interrupted segment of the main artery (Fig. 5), although satisfactory

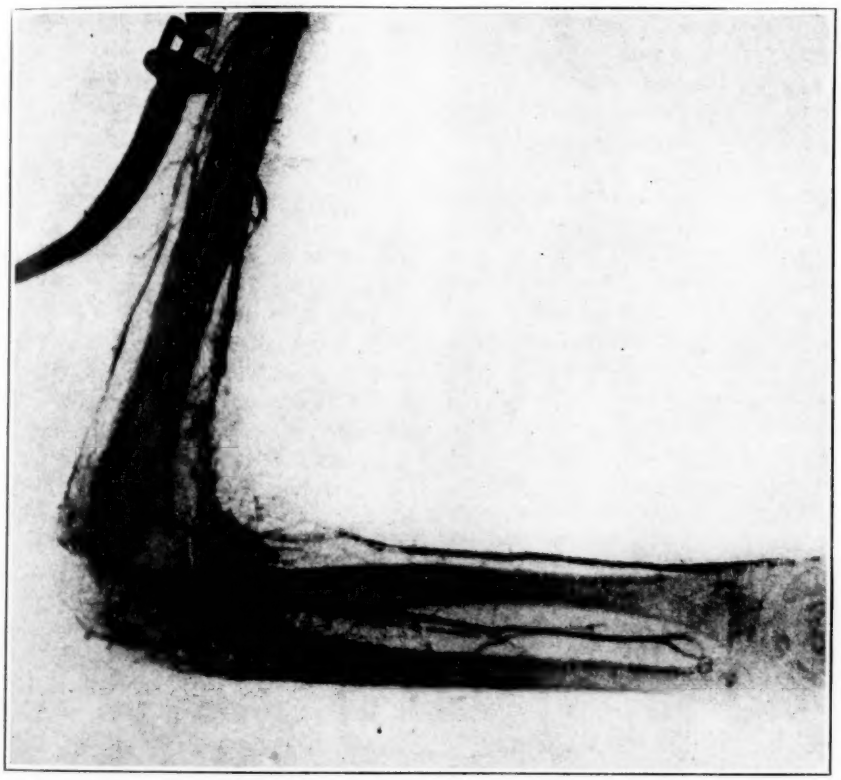

FIGURE 5. *Arteriographic Study in a Case of Volkmann's Contracture. Note the segmentary spasm of the lower end of the brachial and the upper ends of the radial and ulnar arteries (Leveuf[12]).*

*A 3-cm. to 5-cm. segment of the contracted artery is removed, with simple ligation of both free ends.

collateral circulation had eventually been established. If the artery is going to maintain a contracted state, it is of no value as a blood carrying channel, and the removal of this contracted segment is not a circulatory loss.

Leriche et al.[9] urge arterectomy on the ground that a constricted artery that has no blood flowing through it but still has its sympathetic fibers running through its adventitia is in effect not an artery at all, but is an abnormal sympathetic nerve. To my mind, the most surprising feature in the results obtained in this group of cases is the improvement obtained in patients operated on comparatively late. Du Pan[13] reported a case in which arterectomy was performed over three weeks after the onset of symptoms, with complete recovery except for slight hypothenar and interosseus atrophy. This fact throws some doubt on Griffiths's conclusion that irreparable damage is done within the first twenty-four hours; he was probably influenced in this belief by the fact that flexion deformity of the fingers is one of the earliest signs to appear, but at this stage it could hardly be the result of cicatricial contraction. In discussing Massart's paper, Mutuel[14] brings up this point. He cites the observation that with a patient asleep or under an anesthetic, pressure of a blood-pressure cuff causes the fingers to flex. Browne[15] has spoken of this flexion as the position of "physiologic rest," and I believe that its assumption in the early stages simply means that the patient naturally assumes the position that is most comfortable and causes the least traction on the disturbed area. The subsequent permanent flexion deformity is the result in part of the fact that fibrosis occurs with the fingers in flexion to begin with; this deformity is further developed by subsequent cicatrization.

Discussion

The mechanism of production and of the possible results of arterial spasm is a field new enough to be filled with opportunities for further study and many interesting possibilities, which are by no means limited to various circulatory disturbances of the extremities; to keep this discussion within reasonable bounds, however, one must for the moment curb any impulse to speculate, and consider only the subject at hand. It has probably always been taken for granted that arterial circulation is adequate unless the main artery is plugged, divided or shut off by external pressure, and therefore the realization that complete ischemia can be developed by the action of the artery walls is rather shocking. Still more interesting is the fact that the major arteries are by no means essential, and that the collateral circulation holds the balance between life and death of the peripheral tissues. Volkmann's contracture is a result of a relatively temporary subtotal ischemia, which may be initiated by any injury or circulatory disturbance that sets this mechanism into action.

An interesting sidelight is that, because in most cases this complication is probably the result of the initial injury, many surgeons have been unjustly accused of unskillful treatment. Du Pan,[13] after reporting his case, confesses his guilt in this respect. He relates that he had always prided himself on the fact that this complication had never occurred in his clinic, a record that he attributed to painstaking care in reduction and immobilization. He had looked with privately raised eyebrows on the occurrence of Volkmann's contracture in the hands of his confreres, supposing that it would not have happened under his care. His chagrin can be imagined when, in spite of his best efforts, the contracture occurred in his own case. He concludes, "Désormais, je serais plus indulgent!"

That this mechanism is the proximate cause of Volkmann's contracture is attested by the universal finding of segmentary arterial spasm in all cases in which the artery is surgically exposed during the acute stage. What could not be so easily demonstrated but must logically be considered a key factor is vasoconstriction of the collaterals when the resulting ischemia is total or nearly so. Arterectomy affords all the elements of completely rational treatment because it removes a segment of artery that is not contributing to the circulation but is a source of abnormal sensory impulses, and because it completely interrupts the sympathetic reflex arc both centrally and locally, and thereby most effectively produces vasodilatation of the collaterals.

Conclusions

Volkmann's ischemic contracture should be divorced from its association with supracondylar fracture of the humerus. It is the result of a nearly complete ischemia produced by arterial spasm of the main artery and the collateral circulation.

Interruption of the sympathetic reflex arc is the rational treatment.

Arterectomy gives the best results in stubborn cases.

520 Commonwealth Avenue

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CIRRHOSIS OF THE LIVER COMPLICATED BY PERSISTENT RIGHT HYDROTHORAX AND ASCITES

Report of an Unusual Case

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FROM time to time, cases of cirrhosis of the liver complicated by right hydrothorax have been reported, but the case described below is unusual because of the huge amounts of fluid removed and the great number of tappings both pleural and peritoneal required during the course of the patient's illness. Christian[1] reported a case of hepatic cirrhosis with left-sided hydrothorax requiring a total of nine taps ranging from 800 to 2400 cc. for each tap. Goodman[2] described a case in which an accident had caused a diaphragmatic hernia and in which the extended omentum acted as a ball valve, causing "pleural ascites" in a patient with cirrhosis. Seven taps were necessary, with a total of 20,450 cc. removed. Individual taps yielded 650 to 5200 cc. Sears and Lord[3] described a case of ascites from which "during the last two months of his [the patient's] life between sixty and seventy-two quarts were three times withdrawn." Clerc, Debray, Chassagne and Soullard[4] reported a case of long-standing cirrhosis requiring one hundred and fourteen abdominal taps over a period of ten years. The frequent tappings and recurring ascites had caused a remarkable distortion of the abdomen. The amounts of fluid removed were not given.

Heart failure has long been recognized as a cause of right pleural effusion. Garvin[5] described such a case in which forty-five taps, averaging 1065 cc. each (total 47925 cc.), were required. For one period of nineteen days, a tap was necessary daily, each one yielding about 1000 cc. The most fluid removed at one time was 1850 cc.

There are many other causes for recurrent hydrothorax, but the case reported below is unusual because the number of taps and the amount of

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fluid removed far exceed any that I have been able to find in the literature. Even though permission for an autopsy was refused in this case, many diagnostic data, including biopsy, were obtained during the illness, so that the diagnosis is reasonably certain.

Case Report

H. L. D., a 40-year-old physician, had been in robust health about a year before his first hospital admission (November 4, 1939). At 14, the right hip had been incised and drained for a questionable tuberculosis. The patient had recovered from this satisfactorily. At 28, he had had several attacks of pain under the right costal margin, but none since. The past history was otherwise not remarkable. There was no history of excessive alcoholic intake, although the patient used whisky moderately. The family and marital histories were noncontributory.

For 10 months before admission, the patient had noticed a tendency toward easy fatigability but had no definite complaints. He complained of vague, mild abdominal discomfort, but there was no localized pain of any sort or jaundice at any time. During the 2 weeks before admission, he noted an increasing tendency to easy fatigue and a gradual enlargement of the abdomen, so that his trousers became uncomfortably tight. It was believed that ascites was present, and he entered a hospital for peritoneoscopy and further study. Examination of the blood and urine was negative. The blood Hinton reaction was negative. X-ray films of the abdomen and chest revealed no abnormalities, except for the characteristic abdominal haziness associated with the high diaphragms caused by the ascites. Peritoneoscopy showed "a tiny liver, the entire surface of which was made up of irregular clusters of small nodules"; no biopsy was performed. The patient was discharged on the following day, with a diagnosis of hepatic cirrhosis. The abdominal wound drained slightly for a few days and then entirely healed. The fluid in the abdomen thereafter seemed to decrease until none could be demonstrated. The patient remained at home leading a fairly sedentary life on a high-vitamin, high-carbohydrate regime, but in spite of this he noted increasing fatigue. He lost about 20 pounds in weight during the next 2 months.

On January 6, 1940, the patient noted marked increasing dyspnea, and on examination the following morning he was found to have a massive pleural effusion on the right. He again entered the hospital on January 7. Physical examination showed signs of fluid in the right chest, a barely palpable liver edge and slight icterus. The spleen was not felt. The urine and blood were normal. The serum protein was 7.8 gm. per 100 cc.; the albumin was 3.1 gm. and the globulin 4.7 gm. The benzoic acid (Quick) test showed decreased liver function; the icteric index was over 100. Two thousand two hundred cubic centimeters of straw-colored fluid was removed in two taps. Culture showed no growth. The fluid protein was 0.72 gm. per 100 cc. X-ray examination of the chest after removal of the fluid showed normal lung fields and no apparent cause for the fluid. The patient was discharged after 4 days.

On January 13, he was again admitted because of dyspnea caused by hydrothorax on the right. He remained in the hospital for 12 days, and was tapped 3 times, with the removal of 2400, 3800 and 3300 cc. of fluid. The fluid consistently showed a specific gravity of 1.010 to 1.012, and was of an amber color. No tumor cells were found in the centrifuged sediment. There was a small amount of bile in the urine. At the patient's request, it was decided to perform any further tappings at his home, and he was discharged after 12 days. There was still no evidence of accumulation of fluid in the abdomen.

From January 27 to March 1, a right thoracentesis was required every 2 days for relief of dyspnea. The smallest amount of fluid removed at one tap was 1600 cc.; the greatest amount at one time was 4100 cc. The tappings usually yielded 2800 to 3500 cc. Except for one gastrointestinal upset characterized by chills, fever and diarrhea, for which he was hospitalized a few days and which subsided spontaneously, he was fairly comfortable when not bothered by dyspnea caused by the hydrothorax. When this was marked, the liver edge was easily palpated, and the edge of the spleen could occasionally be felt. Sediment from the fluid again showed no tumor cells on repeated sections. There were an abundance of eosinophils and mesothelial cells and a few leukocytes, which were interpreted as being a reaction to the frequent tappings. The serum protein on February 7 was 6.1 gm. per 100 cc.; the albumin was 3.1 gm., and the globulin 4.7 gm. The icteric index was 15. The specific gravity of the chest fluid was usually recorded as 1.007 or less. Venous pressure in the right arm on March 8 was 75 mm. of water.

On March 11, the patient entered the Peter Bent Brigham Hospital for further study. Following complete removal of the fluid in the right chest, a bronchoscope was passed. No abnormalities of the bronchial tree could be found in the lungs. X-ray studies of the lungs following lipiodol injections likewise showed no abnormal findings. A swallow of barium revealed very marked varices at the lower end of the esophagus. There was no evidence of heart disease. Since these studies revealed no evidence of cancer in the pleura, mediastinum or lungs, it was believed that the recurrent right hydrothorax must be associated with the cirrhosis of the liver, which had been proved by peritoneoscopy and reduced liver-function tests.

With the exception of 2 days during March, it was necessary to tap the right chest every day. The tappings yielded 1200 to 4100 cc. each, usually about 2400 cc. This meant that the patient was constantly accumulating approximately 100 cc. per hour in the right chest. The left chest and abdomen remained free of fluid. There was no peripheral edema at this time. There were twenty-five consecutive daily taps.

During April and the first half of May, it was necessary to tap him only every 2 days. The decision to tap the chest was determined by the patient's discomfort. The amount of fluid removed usually averaged around 2800 to 3000 cc. His general condition remained essentially unchanged. During the latter part of May and early part of June, he was tapped every day or every 2 days. From June 16 to July 30, taps were performed daily. The patient was not tapped on July 31. From August 1 to September 30, he was tapped daily. Thus, with the exception of 1 day, the patient required daily right thoracenteses for 106 consecutive days. Most of these procedures were done in the home, but during the latter part of August and in early September the patient felt well enough to travel by automobile to the hospital for the daily chest tap. A total of 1500 to 2500 cc. was the usual yield of each tap.

Because of the apparently endless flow of fluid into the chest and because generalized anasarca was beginning to develop, he was again admitted to the Faulkner Hospital on September 12. On July 12, the serum protein

had been 4.8 gm. per 100 cc., with an albumin of 2.4 gm. and a globulin of 2.4 gm. On September 17, the serum protein was 6.3 gm. per 100 cc., the albumin was 2.6 gm., and the globulin 3.7 gm. Since the patient was quite obviously not improving, further steps were deemed advisable, to stop the recurring right hydrothorax. It was reasoned that following the removal of 2000 to 3000 cc. of fluid from a closed structure such as the chest, where there is normally a pressure less than atmospheric, there must be an increase in negative pressure. This partial vacuum would tend to suck even more fluid into the pleural space. If, therefore, the fluid were replaced by as much air as necessary to bring the pressures to nearly neutral, there would be less tendency for the fluid to reaccumulate in the right chest. Therefore, during the next few thoracenteses, approximately the volume of about half the total fluid removed was replaced in the form of air. After this procedure had been repeated about five times, the amount of fluid began to decrease. Associated with this, there was some slight pain on deep breathing on the right side, and there was a slight rise in temperature to a maximum of 100.4°F. This gradually subsided. A slight right pleural friction rub was associated with the pain and fever. The amount of fluid aspirated from the chest gradually diminished, until on October 7 only 350 cc. was removed. Complete removal of the fluid resulted in pleuritic pain, and therefore, a cushion of fluid was left after each tap. This was the last chest tap that was necessary for 4½ months.

The patient was once more discharged home at his own request, and his condition remained essentially unchanged for the next 4 days. However, he soon began to notice some swelling of the abdomen, and on October 13, his first abdominal paracentesis yielded 5000 cc. of straw-colored fluid, which did not clot on standing. The abdominal fluid appeared to be entirely similar to the chest fluid that had previously been obtained. The specific gravity was low, as was the protein content of the fluid.

During the next 2½ months, it was necessary to perform abdominal paracenteses about every 4 to 6 days, to relieve the patient's discomfort; 2000 to 4000 cc. was the average yield of each tap. During January, 1941, it was necessary to tap the abdomen every other day.

On January 18, the patient was admitted to the Faulkner Hospital for an omentopexy and ligation of the splenic artery. This was undertaken because he had become discouraged with his long illness and because the accumulation of fluid seemed to be rapid. At operation, no adhesions were found in the abdomen or about the spleen. The liver appeared normal in size, and the surface was extremely hard and covered with very many bluish nodules. A biopsy of the liver showed, microscopically, numerous broad, fibrous trabeculations separating the liver substance into irregular lobes. Wherever the portal structures could be identified, there was always a broad connective-tissue zone and, in addition, an irregularly distributed fibrosis throughout the structure. Definite hyalinization was not found, although there were some areas suggestive of it. The pathologist's diagnosis was "cirrhosis of the liver: to be regarded as unclassified, although suggesting Laennec's type." Because of technical difficulties and the large spleen without adhesions, the splenic artery was not tied. The omentopexy was completed, and the abdomen closed without drainage. Eight paracenteses were required while the patient was in the hospital after the operation; he returned home on February 11.

At home, it was necessary to tap the abdomen every day or every other day (1500 to 2000 cc. each tap) until February 22, when the patient complained of dyspnea and discomfort in the right chest. Because of the markedly thickened pleura from the previous thoracenteses, it had for several months been nearly impossible to determine the presence or absence of fluid in the chest. However, a chest tap revealed 3000 cc. of the usual straw-colored fluid. During the next 4 days, daily chest taps revealed a gradually diminishing accumulation of fluid in the right thorax. The abdomen had to be tapped only once during this time, and only 700 cc. of fluid was removed. However, with the cessation of the fluid in the right pleural cavity, abdominal paracenteses again had to be resumed every 2 to 4 days. Usually, 2500 to 3500 cc. of fluid was removed with each tap. More fluid in the abdomen caused great discomfort. Profuse draining often occurred following abdominal taps, and the patient occasionally leaked freely enough through the wound to make tapping unnecessary for an extra day. His condition continued about the same until the end of April. On one occasion in April, he again complained of discomfort in the right chest. A thoracentesis yielded about 100 cc. of grossly purulent material. A stained smear showed this material to contain innumerable leukocytes and a few staphylococci and streptococci, which may have been contaminations; no culture was taken. The patient showed little clinical evidence of empyema, and it was not necessary to tap the chest again.

During the course of the illness, the urinary output was quite scanty. On examination, the urine was usually highly concentrated but otherwise not remarkable. Various diuretics of the mercurial and xanthine derivatives were tried without effect. During March, April and May, 1941, increasing edema of the lower limbs and abdominal wall gradually developed. About April 15, the patient began to notice some ecchymoses of the skin of the legs and trunk. There was also some transient pain in many of the small joints of the body. A few days later, the urine became a muddy wine color, and gross hematuria was noted. The urinary sediment contained many red and white blood cells, and remained so for the duration of the illness.

The course was steadily downhill from then on. Abdominal taps were required every 2 or 3 days. The amount of fluid removed ranged between 600 and 3400 cc. The patient was often very insistent on being tapped, even though it seemed unnecessary at the time. The omentopexy had apparently failed to benefit him.

On May 29, he gradually lapsed into a comatose state, and died on June 1.

Summary

A case of cirrhosis of the liver, proved by biopsy and without any clinically demonstrable pathology of the lungs, mediastinum, pleura or heart, is reported; recurrent right hydrothorax necessitated two hundred and eleven thoracenteses for the removal of a total of 467,100 cc. of fluid from the right chest. In addition, it was necessary to perform eighty-seven abdominal paracenteses for the removal of a total of 214,580 cc. of ascitic fluid. The ascitic fluid and the chest fluid appeared to be similar. With the exception of one day, it was necessary to tap the chest daily for one hundred and six consecutive days. The greatest amount of fluid removed from the chest at any one time was 4100 cc.

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ARGYRIA CONFUSED WITH HEART DISEASE*

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CYANOSIS is a common finding in both congenital and acquired heart disease. When marked, it is detectable not only in the skin (especially in the most distal parts of the body such as the hands, feet, ears and nose), but also in the mucous membranes and the tongue. Argyria also produces a discoloration of the skin, resulting in a slatelike appearance that may closely resemble the cyanosis of heart disease. Our attention was called to the confusion between these two states by the mistaken diagnoses that were made on several occasions in the last few years. It is evident that the error of overlooking argyria and misinterpreting the discoloration of the skin as being due to the cyanosis of heart disease is a grave one but easily avoidable. Furthermore, the gradual and insidious development of argyria itself is a condition that is entirely unnecessary and preventable. It is because of these simple facts that we believe it appropriate to report the cases discussed below.

It is not our purpose to review the literature on argyria or to go into the mechanism or chemical background of its development. Because of the apparent harmlessness of even marked degrees of argyria, the great majority of cases are never reported. All physicians at one time or another have seen cases, so that the sparse statistical reviews in medical journals can give only a meager picture of its prevalence. We were able to find only one reference in the recent literature in which the presence of argyria led to the mistaken diagnosis of heart disease.[1]

The discoloration in argyria may be of two types: local, such as that around the eyes due to instillation of various forms of silver solutions into the lachrymal ducts, and generalized discoloration of the skin. The latter is apt to result from the absorption of silver through the nasal and gastrointestinal mucosa, such as that following nasal instillations, or by the injection of silver arsphenamine in the course of antisyphilitic therapy. Gaul and Staud[2] point out that the degree of discoloration depends directly on the extent and duration of the solar or artificial radiation and the amount of silver present in the skin. In following patients receiving antisyphilitic therapy, the authors believed that the clinical detection of argyria occurred when a total of about 8.0 gm. of silver arsphenamine had been given parenterally. It is well known that parts of the body exposed to the light are more profoundly discolored than areas protected by clothing. It is also of interest that the regional intradermal injection of a solution containing 1 per cent potassium ferrocyanide and 6 per cent sodium thiosulfate produces a local and permanent disappearance of the slatelike skin discoloration.[3] In fact, this procedure has occasionally been used therapeutically. The discoloration from bismuth may closely resemble that from silver, but the former is prone to recede spontaneously in three to six months, whereas the latter remains unchanged indefinitely.[4]

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Case Reports

CASE 1. A 7-year-old boy was brought in for examination on January 5, 1934, with the diagnosis of congenital heart disease. He was supposed to have had a bluish discoloration of the skin, especially around the nose and lips, since birth and was treated all this time as a case of congenital heart disease. His father stated that the skin of the rest of the body appeared normal until a few months prior to the visit, and since then the discoloration had involved the entire body. The child otherwise felt well, went to school and played normally, except that he grew fatigued more easily than other children. The pediatrician had always cautioned the parents about the child's activities, and the entire household lived under the constant dread that organic heart disease entails.

Physical and x-ray examinations revealed a heart of normal size. There was a Grade I apical and basal systolic murmur, but no other abnormalities. Electrocardiograms were normal. The general state of nutrition was only fair, and the urine was entirely normal. There was no clubbing of the fingers. The important finding was the diffuse grayish-blue line of the skin, most marked in the face but moderate in degree over the rest of the body.

It was this discoloration that had been interpreted as cyanosis and had led to the diagnosis of congenital heart disease. It quickly became evident that the color was quite different from what is seen in organic heart disease. Furthermore, the mucous membranes of the tongue, mouth and conjunctivas appeared normal; if the high degree of discoloration had been due to congenital cardiac cyanosis, one would certainly have expected to find evidence of it in these structures. At this point, on direct questioning of the father, it was learned that since the age of 3 months, when the child had a slight nasal cold, he had been given almost daily instillations of silver nitrate or Argyrol in the form of drops or spray to prevent sinus infection. In November, 1933, he had been given a half dropperful of silver nitrate solution in each nostril three times a day for a week, and off and on ever since. During the 1st year or so of this silver treatment, the mother was carrying out the doctor's orders. Subsequently, it was more or less her own method of prophylaxis that motivated treatment. However, she had never been told about the potential danger, or to stop the nose drops.

The entire situation was explained to the family, and it was made clear that the heart was perfectly normal and that the boy should never use silver in any form again. He has been well ever since, although he continues to show the marked bluish discoloration of the skin.

Case 2. A 15-year-old girl was seen on April 5, 1941, because of a general run-down condition, rapid pulse, loss of weight and slight fever of several months' duration. Although the physician in charge was not greatly concerned about the situation, there was some suspicion of the possibility of a smoldering rheumatic fever or subacute bacterial endocarditis. She had been seen by numerous physicians because of recurrent slight grippelike infections and a general feeling of asthenia. Many tests, including blood cultures, urinalyses and chemical analyses of the blood, were normal, and x-ray studies were negative. The basal metabolic rate was found to be −18 per cent, and for this reason 1 gr. of thyroid was given three times daily. This was discontinued after a few weeks. More recently, the patient had had a mild sore throat, bilateral otitis media requiring paracentesis, and slight cervical adenitis. Most of the symptoms subsided, although she tended to run a temperature slightly over 99°F. At various times during these few months, attempts were made to have the child get out of bed and resume moderate activities. Each time, the mother and a physician noted that after a little play the pulse would be rapid, and what was interpreted as a cyanotic tint to the skin appeared.

Examination revealed a tall, thin, attractive-looking girl with a very faint bluish tint to the skin of the face. The heart was entirely normal, except for a very faint apical systolic murmur.

It quickly became apparent that the main problem was a psychiatric one and involved a difficult relation between mother and daughter. Because of the suspicious appearance of the skin, a direct inquiry was made concerning the use of nose drops. It was then learned that for 5 or 6 years the girl had received almost daily instillations of silver nitrate solution. The mother admitted using about 2 or 3 ounces of such solution a year. This had been unsuccessful in preventing colds and sinus infections to which the patient was subject.

When the entire situation was explained to the mother and the family physician, their apprehension concerning the so-called "cyanosis" was relieved. The importance of the physical aspects of the problem was minimized, and after an appropriate conversation with the child and the mother a better psychologic adjustment was obtained. The result was that the child resumed her schooling and returned to good health. In this case, the disfiguration from the argyria was almost nil, since it could hardly be detected. Its recognition, however, prevented an irretrievable injury to a young girl whose future would otherwise have been greatly handicapped.

Case 3. A 37-year-old woman was seen on March 23, 1938. She complained that she had no "pep" and that her fingers were blue. She had had both rheumatic fever and chorea in childhood, and during the last several months had noticed that her heart "turned over" at times. She had been put to bed by her physician because it was thought that she had heart disease. There was no history of dyspnea or pain in the chest.

Examination showed a tall, thin woman with a somewhat slatelike discoloration of the face. The heart was not enlarged, but there was a slight apical systolic murmur. The blood pressure was 134/85. Aside from the murmur, nothing abnormal was found except that the fingers were distinctly blue. Electrocardiographic tracings were normal, and the vital capacity of the lungs was 3400 cc.

It was obvious that this patient had no organic heart disease. The discoloration of the skin was of the type seen in argyria, and with this in mind, it was learned on direct questioning that for the previous 5 years she had taken seven drops of a 10 per cent Neosilvol preparation in each nostril every night. This procedure had been carried out on the advice of a nose-and-throat specialist because of chronic sinus infection.

In this case, the correct interpretation of what the physician regarded as cyanosis led to the diagnosis of no organic heart disease, despite the past history of rheumatic infection.

Case 4. A 50-year-old woman was seen on February 3, 1939, complaining of weak spells with peculiar sensations in the chest, and a feeling "as if the blood were rushing to her head." There was no dyspnea or difficulty on walking, and no history of previous rheumatic infection.

Examination revealed a faint grayish-blue tint to the skin of the face, and a distinctly bluish discoloration of the base of the nails. The blood pressure was 135/88, the heart was not enlarged, there were occasional extrasystoles, and the first sound at the apex and the second sound in the pulmonary area were accentuated. There was a definite, but very short, presystolic murmur at the apex. The vital capacity was 1900 cc., and the electrocardiogram showed a prominent auricular complex, or P wave. The remainder of the examination was entirely negative.

The appearance of the skin aroused the suspicion of argyria, and on further questioning, it was learned that for 4 years the patient had been using a Neosilvol spray twice daily. She stated that she squeezed the bulb of the atomizer four times into each nostril with each treatment. Immediate and complete discontinuance of all silver medication was urged.

In this case, there was evidence of well-compensated organic heart disease, but the detection of argyria helped to minimize the gravity of the situation, for there was no evidence of heart failure.

Case 5. A 72-year-old physician was seen on August 7, 1940. During the previous several months, he had noticed increasing shortness of breath, swelling of the ankles and spells of discomfort in the midsternum on hurrying.

Examination showed a blood pressure of 185/85, slight enlargement of the heart and a coupled beat, but there were no murmurs. There were a few rales at the right base and considerable soft, pitting edema of the legs. Electrocardiographic tracings showed delayed conduction

time (PR interval, 0.24 second) and coupled beats due to extrasystoles. There was marked slatelike discoloration of the face, but the scleras were not involved.

This patient had congestive heart failure on a basis of coronary-artery sclerosis and slight hypertension. However, the discoloration of the skin was obviously due to argyria, and it was learned that 20 years previously he had begun using nose drops containing either silver nitrate or Argyrol. He continued this more or less regularly for 10 years, but did not notice the change in the skin until a few years after the instillations had been discontinued.

The heart failure progressed despite appropriate treatment, and the patient died in March, 1941. In this case, the marked argyria was an incidental finding, and had no effect on the cause or prognosis of the basic organic heart disease.

Discussion

In these 5 cases of argyria, mistakes in diagnosis or interpretation of so-called "cyanosis" had previously been made. In 4 cases, faint or marked discoloration of the face or fingers had been regarded as cyanosis of circulatory origin. In all but 1, the fact that nose drops of silver preparations had been used for long periods had been entirely overlooked by the physicians in charge, and had not been mentioned by the patients or their families until direct inquiry was made. In 1 case, the marked slatelike tint, which had been present since infancy, was interpreted as cyanosis of congenital heart disease. In 2 other cases, a milder bluish tinge of the skin brought up suspicions of acquired heart disease. In none of these 3 cases was any evidence of organic heart disease detectable. Of the 2 remaining cases, one patient had a slight, well-compensated mitral stenosis, and the other, heart failure on the basis of hypertension and coronary-artery sclerosis; in both, the "cyanosis" was due entirely to argyria.

It can be readily seen from these experiences that argyria is quite common and often overlooked. It is essential to recognize this fact to avoid serious errors in diagnosis and prognosis. Argyria can naturally be present either with or without organic heart disease. There seems to be no physical handicap that results from even marked argyria, but very great harm can be done to the psyche and personality of the patient from the cosmetic discoloration of the skin. When argyria accompanies organic heart disease, the prognosis is obviously a good deal better than if the condition is misinterpreted as cardiac cyanosis.

No doubt, there is some advantage in using silver preparations for short periods. However, there appears to be no reason to continue the use of nose drops containing silver over the course of months or years when it is realized that the insidious onset of an irreversible and ugly discoloration of the skin may result. Patients and their families should be cautioned very carefully against this danger. It might even be wise to write the expression "do not refill" on all prescriptions containing silver salts.

Summary and Conclusions

Five cases of argyria are presented in which the condition was entirely overlooked for months or years, and the discoloration was misinterpreted as definite or possible evidence of organic heart disease. In one case, it was so marked since infancy that the child was treated for many years as a patient suffering from congenital heart disease. In another, because of bizarre symptoms and slight fever, the possibilities of smoldering and active rheumatic fever or subacute bacterial endocarditis were considered. In another case, because of the past history of rheumatic fever, the possibility of rheumatic heart disease had been entertained. The remaining patients had organic heart disease, but the so-called "cyanosis" was not due to heart failure.

Argyria must be distinguished from the cyanosis of heart or pulmonary disease. It has a peculiar, grayish, slatelike tint, in contrast to the purplish hue of cardiac cyanosis. It is most frequently confined to the parts of the skin exposed to light, the tongue and mucous membranes, which are generally involved in cyanosis due to circulatory disease, being unaffected.

It is evident that argyria is not uncommon, and if it is not recognized, it may lead to a serious error in the diagnosis or management of heart disease or both. Finally, because it is an unnecessary and preventable handicap that is insidious in its development, greater caution must be exercised by physicians in dispensing silver preparations.

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HEMOTHORAX COMPLICATED BY INFECTION WITH *CLOSTRIDIUM WELCHII**

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WITH the increasing mechanization of modern life, the occurrence of hemothorax and hemopneumothorax resulting from penetrating and nonpenetrating injuries has become so frequent that the conditions are usually sought for and recognized. Moreover, the possibility of infection as a complication of these injuries is generally appreciated, and when it occurs, measures are taken to deal with it. However, infection of a hemothorax by the gas-producing micro-organisms is a complication not frequently described in civil practice, most of the reported cases having occurred as war injuries. Such infections may be overlooked or the symptoms misinterpreted, since the production of gas by these micro-organisms in the hemothorax may simulate hemopneumothorax, with a small but constant bronchopleural fistula.

It is the purpose of this paper to discuss this complication of penetrating wounds of the thorax and to report our experience with such a case at the Boston City Hospital.

That the condition is rare is apparent from the literature, for various reviews[1, 2] of infection with *Clostridium welchii* do not mention pleural involvement. Others[3, 4] mention it briefly, citing a single case, without further discussion. Elliott and Henry[5] analyzed their findings in an excellent review of 87 cases in World War I. They found that under war conditions 25 per cent of all hemothoraxes became infected, and 44 per cent of these were infected by the gas-producing bacilli. Hence 10 per cent of all hemothoraxes were infected by gas-producing bacilli, and 33 per cent of these were fatal. The diagnosis is made by culture and smear of the aspirated fluid, although an odor of hydrogen sulfide may be accepted as very suggestive without the culture. Because the infection may remain localized in one part of the blood clot, a negative culture is sometimes obtained; therefore, repeated thoracenteses should be done in any suspicious case. Clinically, for the first twenty-four to forty-eight hours, these patients present a picture of a mildly infected hemothorax; the temperature is usually no more elevated than that in a simple uninfected hemothorax, but the pulse is rapid beyond expectation.

The cases observed by these authors may be divided into five main types, depending on the predominance of gas production or toxicity: the acute pneumothorax, with overwhelming gas production, which appears clinically as a sudden tension pneumothorax with or without hemorrhage and may progress to a fatality in two or three days; the fulminating septic, in which delirium and jaundice are outstanding and which may be fatal in two or three days; the progressive pneumothorax, whose main feature is a free or localized collection of gas, symptoms and signs becoming obvious after the fourth or fifth day following injury; the progressive toxic, in which symptoms become apparent at the same time as those of the progressive pneumothorax and in which jaundice, restlessness and delirium are prominent; and the chronic, which progresses in the same manner as the usual infected hemothorax, without marked gas formation or toxemia.

In treating such infections, these authors have found that radical surgery is most successful. Attempts to avoid opening the thorax proved largely unsuccessful probably because the large masses of infected clot were not removed. Some patients may do well with closed drainage, or the maneuver may be needed as a temporary measure to decompress those suffering severe mechanical disturbances or those who are markedly toxic; as a general rule, however, the open operation is advised.

In a brief discussion of this condition, the reports of the Medical Department of the United States Army[6] ambiguously state that "open drainage was generally held to offer the best chance of recovery from this type of pleuritis, though closed drainage would have been more efficacious."

Two other reports of *Cl. welchii* infection of the pleura were found. Bader and Müller[7] report a case in which the infecting organism was introduced at the time of thoracentesis, a method of infection that they consider not uncommon. In the cases reported by these authors, this seems reasonable, but from our experience at the Boston City Hospital we cannot concur in their opinion concerning frequency. They believe that the opening of the pleural cavity and the resulting aeration

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are the most valuable features in the treatment. Porzecanski and Franchi,[8] report a case following a gunshot wound of the chest, in which the patient was treated by rib resection and recovered.

At the Boston City Hospital, many cases of penetrating wounds of the chest are admitted annually, yet this complication has been seen but twice in recent years. On one occasion, a patient with a stab wound of the chest showed *Cl. welchii* in the first culture of the hemothorax fluid two days after the injury. However, he failed to show signs of infection, subsequent cultures of the fluid were negative, and recovery was uneventful. The second case is presented in detail because it showed definite infection of the hemothorax by *Cl. welchii*, with recovery following early open drainage, after the method described by Dolley and Jones[9] for treatment of putrid empyema secondary to rupture of a lung abscess.

Case Report

T. L. (B. C. H. 1006093), a 34-year-old man, was admitted to the hospital on November 25, 1940, with the complaint of shortness of breath of 2 days' duration. He stated that 5 days before admission he was stopped on the street by two men, who, having been refused money, stabbed him in the left chest. The wound seemed superficial, and he cared for it at home with the help of his wife, who was a trained nurse. He was able to work as a tailor, although 2 days before admission he was moderately dyspneic. This symptom increased until the day before admission, when it was severe enough to keep him in bed. Despite bed rest, the dyspnea increased, and he entered the hospital.

On admission, the patient was acutely ill, anxious, moderately cyanotic and markedly dyspneic. The extremities were cold and moist, the pulse was 120, the temperature was 98°F., and the respirations were 38. The blood pressure was 145/90 and paradoxical between 145 and 120. To the left of the sternum in the 2nd interspace, there was a 2.5-cm. laceration, which grossly appeared clean and through which there was no exchange of air. The trachea was deviated far to the right, and the apex impulse was just to the left of the sternum. There was flatness over the lower two thirds of the left chest, with tympany above this. The breath sounds and tactile and vocal fremitus were absent over the entire left side. Otherwise, the physical examination was negative. The white-cell count was 42,000, and the red-cell count was 4,640,000 with a hemoglobin of 85 per cent. The urine contained many red blood cells and had 3 or 4 white cells per high-power field. The impression on admission was that of a left hemopneumothorax with tension.

A thoracentesis was performed immediately, and 1200 cc. of red, odorless blood removed. Following this, the patient felt much better, the pulse was slower and stronger, and breathing was easier. A specimen of the blood from the chest was sent for a routine culture. For 24 hours, the patient was more comfortable, following the administration of oxygen, morphine and a transfusion of 500 cc. of citrated blood. After this interval, however, he slowly relapsed. The displaced mediastinum, which had come back considerably after the first thoracentesis, was again far to the right, the patient was dyspneic and anxious, and the pulse ranged between 120 and 130, the temperature varying between 101°F. and normal. During the 2nd day, the patient had repeated slight chills lasting from 5 to 10 minutes and associated with increased anxiety, but no marked rise in the temperature. Blood cultures taken during two of the chills were negative. About 60 hours after admission, the patient's condition seemed as poor as when he was first observed, and thoracentesis was performed again. This time, the fluid was thinner, of a chocolate color, and had a definite odor of hydrogen sulfide. About 1500 cc. was withdrawn, with immediate improvement; the pulse was stronger, the respirations easier, and there were no more chills. In addition, a moderate amount of gas was withdrawn with the changed blood, which had the same foul odor.

A smear of the fluid was made at once, and many large gram-positive bacilli were seen. Investigation of the fluid sent for culture on the day of admission showed that a large gram-positive bacillus had grown anaerobically, and nothing had grown aerobically. This bacillus showed all the characteristics of *Cl. welchii*.

On this evidence, the patient was taken to the operating room, and under local anesthesia a 10-cm. segment of the 8th rib was resected. Before the pleura was opened, the patient was given oxygen by a closed mask, and a small amount of positive pressure was maintained. The pleura was opened for about 2 cm., and the aspirating tip inserted. About 2000 cc. of foul-smelling old blood, together with many clots, was withdrawn. The pleura was then opened the entire length of the incision, a previously prepared large dressing was applied, and the patient was quickly turned on his back. There was very little sucking during this procedure, and none once the patient was on his back. He was returned to the ward in good condition; the respirations were much easier, and the pulse slowed to 100. He was transfused again, started on sulfanilamide, and given *Cl. welchii* antitoxin. He received 120 gr. of sulfanilamide a day for the first 3 days, and then 90 gr. daily was given for 7 days. During the first 3 days, 100,000 units of antitoxin, as well as intravenous fluids and nasal oxygen, was given. After this, the temperature was normal, and the pulse was 90.

The first dressing was done on the 3rd day, with the patient breathing against positive pressure. There was an obviously shifting mediastinum, and much foul discharge on the dressing. A culture was again positive for *Cl. welchii*. This was repeated on the 5th day, when the discharge was gray and foul. On the 7th day, the mediastinum was fairly well fixed, and a catheter was brought out through the dressing for irrigations, with maintenance of the closed wound by the dressing. On the 9th day, the fixation was sufficient to allow the insertion of large drainage tubes and the use of open irrigations. After 2 days, the foul odor had disappeared, and the drainage was serofibrinous. For irrigations, physiologic saline solution and, later, Dakin's solution were employed. On the 15th postoperative day, a culture of the drainage from the pleural cavity was negative for *Cl. welchii*, and they remained negative on all of several subsequent occasions.

The patient had one episode of right-sided chest pain, with an elevation of the temperature to 101°F. This lasted for 4 days and then disappeared. During this time, there were no clinical signs on the right, and a roentgenogram of the chest showed no abnormality on the right. Apart from this, the course was uneventful.

The patient was allowed up on the 32nd day, and was discharged on the 39th day, with a residual empyema cavity of 20 cc. Two and a half weeks following dis-

charge, the wound was completely healed, and the patient had returned to work.

Discussion

As penetrating wounds of the chest become commoner in civil life, one may expect to see this complication more frequently, and when such injuries occur in military practice the incidence will certainly be greater. Because fresh blood is not a favorable culture medium for *Cl. welchii*, few cases present signs and symptoms of infection within the first twenty-four hours. As the blood ages, however, it becomes an ideal culture medium, and a patient with a chest injury who is apparently doing well may become acutely ill within twenty-four hours. The production of gas by the infecting organism may lead one to believe that he is dealing with a pneumothorax incident to a small perforation, and thus valuable time will be lost if a course of watchful waiting is pursued.

All who have written on this subject, with one exception,[6] agree that the best treatment is early and complete removal of the old blood and clots from the chest by open drainage. Sulfanilamide, x-ray therapy and the specific antitoxin are undoubtedly of benefit, but it is our impression from this case, and from many other cases of anaerobic infection of the pleura,[11] that the aeration accompanying radical open drainage of the infected pleura is of paramount value. The dangers of widely opening, and permitting to remain open, the pleural cavity without adequate mediastinal fixation are appreciated by all thoracic surgeons; however, early open drainage may be necessary as a lifesaving measure and may be performed safely in these cases by the use of the technic described above. Resection of a long length of dependent rib allows complete drainage of the pleural space, and the large dressing obviates too rapid an exchange of air and the resultant mediastinal flutter. Once the mediastinum is fixed, the treatment is that usually given postpneumonic empyema with open drainage.

Summary and Conclusions

A case of hemothorax complicated by infection with *Clostridium welchii* is presented.

A review of the literature reveals that such a complication is rare in civil practice, but common in the surgery of war injuries.

From the cases reported, and from our experience with this case, we believe that early open drainage is the treatment of choice, but that it should be supplemented with specific antitoxin, chemotherapy and x-radiation.

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MEDICAL PROGRESS

THE CHEMICAL MEASUREMENT AND CONTROL OF CLINICAL VITAMIN DEFICIENCY* (Concluded)

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NICOTINIC ACID (NIACIN)

THE occurrence of nicotinic acid in concentrates derived from yeast was reported by Funk over a generation ago. Physiologic interest in the vitamin began when Warburg and Christian[65] found nicotinic acid amide as one of the split products of so-called "coenzyme II." Since then, increasing evidence that this substance is essential in enzyme systems having to do with oxidation in tissues has appeared. It occurs in both coenzyme I and coenzyme II, which participate in several well-defined biologic systems concerned with cellular oxidation. When Elvehjem et al.[66] showed that this substance cured black tongue in dogs and later isolated nicotinic acid amide from concentrates of liver extract, its value in clinical disease soon became apparent. Spies, Bean and Ashe[67] have reviewed the role of this vitamin in the treatment of pellagra and associated deficiencies. The material is even essential for bacteria, as shown by several investigators, including Mueller,[68] who worked with the diphtheria bacillus. Because its biochemical function has been known for some time, it is not surprising that chemical determination of this vitamin is well established.

Since this material is necessary for the synthesis of coenzymes I and II, it is apparent that a large amount must exist in tissues and in blood in the combined form as a coenzyme. Of the two factors, coenzyme I, otherwise known as cozymase, is the more easily estimated. Accordingly, studies of this material in blood usually relate to the content of coenzyme I in the erythrocytes. For example, Axelrod, Gordon and Elvehjem[69] showed that soon after large amounts of nicotinic acid were fed to mammals an increase in the coenzyme I (cozymase) content of the erythrocytes took place.

Coenzyme I in Blood and Tissues

Since certain yeasts specifically require coenzyme I for fermentation, this method of assay has been used, as suggested by von Euler.[70] The determination of coenzyme I can be made simply in the Warburg micromanometric device under carefully controlled conditions. The basis of the method is that, when varying amounts of coenzyme are added to a washed preparation of yeast, the ensuing rate of fermentation is proportional, within certain limits, to the coenzyme I concentration. The measurement involves the rate of evolution of carbon dioxide resulting when the following mixture is allowed to interact: washed yeast, glucose, magnesium or manganese ion and hexosediphosphate, properly buffered at the optimal pH.

This method may be applied to extracts prepared from tissue and from the red cells of the blood. Thus, von Euler and Malmberg[71] found that human red cells contained 20 to 35 microgm. of coenzyme I per gram of fresh red cells. Even higher values were found by Elvehjem et al.[69] for the red cells of dogs deficient in nicotinic acid, namely, 60 to 66 microgm. per gram of fresh tissue, which is the same as that found in normal dogs. However, Elvehjem and his associates observed that in man the normal value of 20 to 30 microgm. per cubic centimeter of blood might increase to 60 microgm. after the injection of 100 mg. of nicotinic acid a day. This was true of both normal patients and those with pellagra. When this high level had been reached after several days of such therapy, and when the nicotinic acid medication was stopped, the cozymase content of the blood gradually decreased to the normal level in the course of a fortnight. These results confirmed similar results of Kohn.[72] Like blood thiamin, the nicotinic acid seems to be converted into cozymase only in the corpuscles. In other words, it is chiefly the erythrocytes that contribute the enzymic activity of the whole blood.

It is evident, therefore, that the study of the blood is not of great diagnostic help because that of normal and deficient animals does not differ significantly. Thus, Axelrod, Spies and Elvehjem[73] found an average value of 85 microgm. per cubic centimeter of erythrocytes for normal people, as against 69 microgm. in patients with mild pellagra. Similarly, in 5 cases of severe pellagra, values ranged between 70 and 90 microgm. per cubic

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The first part was presented in the April 16 issue of the *Journal*.

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centimeter of erythrocytes. It is true, as found by Axelrod, Madden and Elvehjem,[74] that the liver and muscle tissues from deficient animals contain considerably less cozymase than the same tissues from normal animals. In 9 normal subjects, the value per gram of fresh muscle was 382 microgm. of coenzyme I, as against 214 microgm. in 5 patients with severe pellagra. This procedure, however, is not a very practical one under clinical conditions. When nicotinic acid is administered to patients with pellagra, a marked increase in the coenzyme I contents of both the red cells and the muscle occurs, as found by Axelrod, Gordon and Elvehjem and their collaborators.

Vilter et al.[75, 76] showed that marked decreases in coenzyme I or II may occur in severe diabetic acidosis or in leukemia, and perhaps also in roentgen-ray sickness and pneumococcal pneumonia. Evidence is presented that the corpuscles merely store the vitamin, rather than actually synthesizing it.[77] These authors, in fact, have found low values in several severe clinical syndromes, as have Justin-Besançon and his associates.[78]

After the intravenous administration of nicotinic acid, the major part of the free vitamin disappears from the blood in half an hour, according to von Euler and Schlenk.[79] Not over one eighth of the total blood vitamin is in the free form normally. Indeed, Kodicek[80] believes that there may be no free vitamin normally. After hydrolysis, the whole blood yields between 1 and 5 microgm. per cubic centimeter. Kühnau[81] found 2.5 to 4.5 microgm. per cubic centimeter of whole blood, and Patton, Sutton and Youmans[82] 3 to 5 microgm. Although vitamin-deficient patients tended to have somewhat lower values than normal, this finding was not strikingly consistent. Kohn,[83] who suggested that coenzyme should be expressed per volume of corpuscles, observed the equivalent of 10 to 18 microgm. of combined nicotinic acid per cubic centimeter of human corpuscles (or 50 to 90 microgm. of enzyme).

In summary, it is necessary in determinations of cozymase and nicotinic acid, as in those of the two varieties of vitamin B already considered, to have recourse to urinary studies and particularly to vitamin-tolerance tests.

Nicotinic Acid in Urine

Methods are now available for determining colorimetrically the urinary excretion of nicotinic acid, nicotinamide and nicotinuric acid, together with other possible derivatives closely related to these substances. Under ordinary circumstances, it is found, as reported by Rosenblum and Jolliffe,[84] that in twenty-four hours approximately 3 to 10 mg. of these substances is excreted by normal persons. Perlzweig, Levy and Sarett[85] observed that in 5 normal human adults on an adequate diet, the average daily excretion of nicotinic acid derivatives (exclusive of trigonelline) was 1 to 3 mg. Furthermore, daily trigonelline excretion on a diet free of coffee was 20 to 29 mg. but approximately 200 mg. when the diet included coffee. As pointed out below, nicotine excretion by tobacco smokers may complicate the analysis if special precautions are not taken.

In the twenty-four-hour urine of well-nourished subjects, Melnick, Robinson and Field[86] found from 1.7 to 29.3 mg. and Patton, Sutton and Youmans[82] 3 to 5 mg. In the urine of patients with advanced pellagra, Vilter, Spies and Mathews[87] were unable to find nicotinic acid. In less advanced cases, Kühnau[81] found urinary concentrations in the lower range of normal, that is, 64 to 105 microgm. per 100 cc.

Rosenblum and Jolliffe[84] also noted that, in a patient with pellagra, urinary nicotinic acid was very low and ultimately disappeared as the patient continued on a diet low in vitamin B complex. When such a patient was put on a diet high in vitamin B complex, however, the urinary nicotinic acid excretion rose within a day to normal levels, and subsequently on a daily intake of 100 mg. of nicotinic acid, excretion reached a peak of approximately 10 mg. in twenty-four hours. Indeed, Perlzweig, Levy and Sarett[85] found that after the ingestion of doses of nicotinic acid as high as 100 to 200 mg., normal adults might excrete 3 to 19 mg. of nicotinic acid derivatives, mostly in the form of nicotinuric acid. This represented a recovery of from 10 to 25 per cent. At the same time, there was a definite change in trigonelline excretion.

Several other investigators have studied the retention of excessive doses of the vitamin in normal subjects and in patients with pellagra. In normal controls, the postprandial administration of 500 mg. of nicotinic acid led to a rapid increase in urinary excretion, according to Melnick, Robinson and Field.[86] This amounted to 22 per cent of the test dose, and was excreted mainly in the form of trigonelline and nicotinic acid. Even with a small dose of 50 mg., Najjar and Wood[88] found that the urinary concentration increased approximately tenfold within four hours. Using oral doses of from 150 to 300 mg. of nicotinic acid or its amide, Patton, Sutton and Youmans[82] were able to recover about 20 per cent of the dose within three hours; after this time, however, no extra vitamin appeared in the urine. Parallel observations on deficient subjects yielded only 3 per cent. With a test dose of 100 mg. of nicotinic acid, Swaminathan[89] obtained the following in-

structive results, expressed as twenty-four-hour excretions:

Subject	Normal Excretion	Excretion after Test Dose
	mg.	*mg.*
Well-nourished wheat eaters..	6.8	27.9
Well-nourished rice eaters....	3.2	19.7
Poorly nourished persons.....	1.3	9.8
Deficiency patients.....	1.2	5.1

Therefore, the concentration of the vitamin and its derivatives found in the urine is of considerable help in confirming the diagnosis of vitamin deficiency. At present, few determinations are available to indicate whether the so-called "tolerance curve" can be used as a determination of the extent of saturation or unsaturation of the tissues at large. The evidence to date, however, suggests that the vitamin-tolerance curves in these cases, as in those of thiamin deficiency, may be used to measure avidity of the tissues for nicotinic acid.

Several colorimetric methods have been applied to the determination of the nicotinic acid in urine. Most of these are based on color reactions produced by the pyridine ring. Thus, Vilter, Spies and Mathews[87] and Karrer and Keller[90] employed 2,4-dinitrochlorobenzene in the presence of an alkali hydroxide. Similarly, Shaw and MacDonald[91] and Patton, Sutton and Youmans[82] used the reaction with cyanogen bromide in the presence of aniline. Melnick and Field[92] studied the limitations of this method carefully. Ritsert[93] and Pearson[94] and Harris and Raymond[95] have also applied this reaction, the last named using *p*-aminoacetophenone.

More satisfactory is the colorimetric procedure of Bandier and Hald.[96] In their modification, *p*-methylaminophenol sulfate (Metol-Agfa) was allowed to react with nicotinic acid and cyanogen bromide in aqueous solution in the presence of potassium acid phosphate. Under these circumstances, a clear yellow color was obtained that was constant, stable and directly proportional to the concentration of nicotinic acid or of nicotinamide. Several other pyridine derivatives, including trigonelline, failed to give any color. This method has been further modified by Rosenblum and Jolliffe,[84] and by Perlzweig, Levy and Sarett.[85] The method is convenient and is suitable for most clinical research. The final solution may be analyzed chemically with an electrophotometer. Even in urine from heavy users of tobacco or from coffee habituants, this method has given satisfactory results.

Some investigators have used the so-called "V-factor" as a measure of nicotinic acid deficiency. This factor comprises the combined effects of coenzymes I and II and possibly some other unknown related substances. It is frequently measured by a microbiologic test involving the growth of influenza bacilli. Dorfman, Horwitt and Koser[97] applied this method to human blood and urine, and obtained very consistent results. Likewise, Kohn, Bernheim and Felsovanyi[98] have used the procedure in normal and pathologic subjects, including patients with diabetes, pulmonary disease and pellagra. They found a considerable overlapping of the pathologic and normal patients regarding the content of this factor in corpuscles. Consequently, this method is less desirable for most purposes than the chemical tests mentioned above.

The problem of nicotinic acid metabolism is still complicated by a lack of understanding of the metabolic significance of trigonelline, the betaine of nicotinic acid, and other pyridine derivatives that appear in the urine. Some of these may perhaps be derived from foodstuffs, especially those from seedlike sources. The possibilities are so complex as to make the interpretation of urinary data often difficult. Perlzweig and his associates,[85] moreover, have pointed out that there are considerable differences among several species of animals, and therefore one cannot lean too heavily on collateral animal studies in evaluating observations on man.

Vitamin C (Ascorbic Acid)

A great deal of work has been done with the physiology of ascorbic acid, otherwise known as cevitamic acid. Consequently, it is possible to mention only a few selected investigations with which I am familiar. For clinical work, the classic methods of bioassay are not practical because they involve the use of many animals. Such methods on rare occasions may be used to check the specificity of chemical methods. For example, occasionally it may be found in the analysis of certain vegetables that a false titer is given by chemical methods as judged by the effect on the scorbutic guinea-pig tooth. Under ordinary circumstances, however, chemical methods are quite adequate for clinical study.

Methods

The chief chemical procedures used at present employ modifications of Tillmans's[99] original reagent, the value of which depends on the color loss of an oxidation-reduction indicator known chemically as 2, 6, dichlorophenolindophenol. The use of this indicator has been justified by many observations, such as those of Bessey and King.[100] In this method, under standard conditions, the colored titration solution is rapidly reduced in acid

solution to a colorless compound. The reagent thus serves as its own indicator. Ordinarily, metaphosphoric acid is used as an acid-extractant because it has marked protective properties and is inert toward the indicator.

The basis of this reaction, of course, is the striking reducing effect of the double bond that occurs in the molecule of ascorbic acid between the second and third carbon atoms. Accordingly, the test records only the reduced form of ascorbic acid. Indeed, certain discrepancies have arisen because the oxidized form, which is unstable, is not estimated by this procedure. Some of the complications caused by the presence of other reducing substances have been discussed by Bessey.[101]

In general, it may be said that these difficulties have been largely circumvented in assays of blood and urine. The method for blood is well represented by the procedure of Abt, Farmer and Epstein.[102] In brief, plasma from oxalated blood is treated with metaphosphoric acid to remove protein, and the protein-free fluid is titrated with a standard solution of Tillmans's reagent. This procedure requires 2 cc. of plasma. The final titration is made with a 5-cc. microburette. A stock solution of the dye is made up containing 0.2 gm. per 100 cc. For daily use, it is diluted tenfold. It is standardized against small amounts of ascorbic acid.

Various convenient modifications of this method have been made, but Bessey[101] has adapted the technic to photoelectric colorimetry. Furthermore, Mindlin and Butler[103] have developed a micromethod that is satisfactory for children and requires only 0.2 cc. of capillary blood. Characteristic values obtained in the clinic may be found in the article by Pijoan and Klemperer.[104]

The determination of ascorbic acid in urine by the use of Tillmans's reagent has been described by many investigators. Convenient methods are those of Harris and his collaborators[105] for the titrimetric procedure and of Evelyn, Malloy and Rosen[106] for the photelometric procedure.

Of special interest is the determination of vitamin C in the leukocytes of the blood as described by Stephens and Hawley[107] and more recently by Crandon, Lund and Dill.[108]

Blood Content

As stated above, blood analysis is of little clinical value in the determination of the vitamin B complex. The blood ascorbic acid, on the contrary, can yield definite information, although such information must be interpreted in the light of repeated tests. There is a distinct relation between the level of ascorbic acid in the blood plasma and the dietary intake, as shown by many observers. This problem has been studied carefully by Thysell.[109] The problem has been studied further by Farmer,[110] who points out that, in general, certain levels may be assigned to characteristic dietary intakes. Thus, if the diet contains less than 15 mg. a day, the blood ascorbic acid level may be expected to be less than 0.2 mg. per 100 cc.; under 30 mg. a day, less than 0.4 mg. per 100 cc.; under 50 mg. a day, less than 0.6 mg. per 100 cc.; under 100 mg. a day, ranging between 0.4 and 0.8 mg. per 100 cc. If the dietary intake is more than 100 mg. of ascorbic acid daily, the blood ascorbic acid may be expected to fall between 1.0 and 2.0 mg. per 100 cc. Wolff, Banning and van Eekelen[111] believe that for optimal nutrition the blood plasma should contain more than 1.2 mg. per 100 cc.

Thus, although some indication may be had of the general range of vitamin nutrition from the level in the blood, it must be emphasized that this is true only when repeated determinations are made or when groups of individual studies are compared. Butler[112] has pointed out that even in persons who are not in dire danger of scurvy the plasma level may fall to nil at times, although the tissues are tolerably well saturated with the vitamin. In other words, the blood is a carrier system for the vitamin, but the equilibrium is not necessarily reversible, so that the blood level may fall even though the tissues still contain considerable stores of ascorbic acid. Thus, in a study of human experimental scurvy, Lund and Crandon[113] found that on a scurvy-producing diet the ascorbic acid level of the blood plasma fell to zero in forty-two days, and that of the white cells in the blood in one hundred and twenty-two days. Nevertheless, the first definite signs of scurvy did not appear for five months, and the symptoms were not severe for six months. Therefore, several investigators in this field do not agree with the conclusions of van Eekelen, Emmerie and Wolff[114] that the degree of vitamin C saturation can be estimated by a single blood determination.

It is true that, in general, there is a straight-line relation between the initial ascorbic acid content of the blood and the total quantity of vitamin needed to saturate the subject. Nevertheless, most investigators prefer to study urinary excretions under standard conditions to determine the need of the patient's tissues for the vitamin. This problem has been discussed by Portnoy and Wilkinson.[115] One source of trouble is the fact, emphasized by Heinemann,[116] that there is a sort of renal threshold for ascorbic acid. Indeed, urinary excretion is relatively slight until the serum level reaches approximately 1.3 to 1.4 mg. per 100 cc., whereupon a sharp rise in urinary out-

put occurs. Moreover, this threshold seems to be influenced by several factors.

Urinary Excretion

It was recognized several years ago that in the presence of ascorbic acid deficiency the daily urinary excretion is low. The chief point of discussion has been the quantitative one of how low the excretion may go without indicating that frank vitamin deficiency is present. Originally, Harris and his associates[117] concluded that if a subject excretes less than 13 mg. of ascorbic acid a day he is probably suffering from vitamin deficiency. For a subject to be optimally saturated with the vitamin, van Eekelen and Heinemann[118] believe that a daily excretion of 40 mg. should be maintained.

Many investigators maintain that a much surer way of testing subjects is to study their retention after a test dose of the vitamin. Various procedures have been used involving different doses. The most frequent is that of administering 5 mg. per pound of body weight as recommended by Harris and his co-workers.[117] The vitamin is ordinarily given by mouth, and within the following twenty-four hours it is expected that a saturated subject will excrete more than half the entire dose. For larger doses, less is recovered, and for smaller doses somewhat more on a percentage basis. Indeed, van Eekelen and Heinemann found that when 300 mg. was given subcutaneously to a saturated patient it was entirely excreted within six hours.

A convenient combination of blood and urine tests has been developed by Kastlin et al.[119] This method involves the intravenous administration of 500 mg. of ascorbic acid and the observation of the blood and urine responses for four hours. The results of blood and urine are plotted in the form of curves. Thus, in a normal person, the blood level rises from the fasting level of about 0.7 mg. to about 7 mg. per 100 cc., and then falls very gradually. During the same time, in the course of four hours, the urinary excretion should be over 40 per cent of the test dose. By contrast, if a deficiency exists, only a slight rise in the blood level above the fasting level occurs, and this rise is variable and is rapidly lost as the tissues take up the vitamin. Simultaneously, the urinary excretion is less than 20 per cent of the test dose in the course of the four-hour period. These curves are, in essence, vitamin-tolerance curves, both for blood and urine. The simultaneous use of these two body fluids increases considerably the reliability of the results.

Saturation Tests

More complicated procedures have been employed in investigations involving the administration of the vitamin over the course of several days. Gander and Niederberger[120] determined the total quantity of ascorbic acid needed before saturation was reached. This figure is sometimes known as the "saturation deficit." Similarly, standard test doses have been given daily for a number of days until saturation is reached; the number of days required under these conditions has been used as an index of the vitamin C deficiency. Such a method was employed by Jezler and Kapp.[121] In general, however, such methods are too time-consuming to be practicable except in scientific or fundamental clinical investigations.

Clinical Applications

Of course, such tests have additional usefulness in the detection of latent scurvy. Nevertheless, it has become clear as the result of frequent studies by numerous investigators that the dietary is not the only variable involved. Faulkner and Taylor[122] found that in patients with rheumatic and other infections the vitamin C requirement is high and that such patients often lack optimal stores of the vitamin. Pregnancy and lactation also increase the demand for the vitamin. Some of these factors have been reviewed by Robertson[123] and by Perla and Marmorston.[124] Keith and Hickmans[125] have also found marked deficiency of vitamin C in children with rheumatic fever or chronic rheumatism.

In 1927, Aron[126] reported that in scorbutic children cutaneous wounds often failed to heal whereas following vitamin C therapy they healed quickly. Since then, there has been increased interest on the part of surgeons in this problem. Lanman and Ingalls[127] report the case of a six-week-old infant with spontaneous opening of a laparotomy wound in the presence of scurvy. Similar results were obtained by Taffel and Harvey.[128] This problem has recently been studied in man by Lund and Crandon.[113] These investigators concluded that lack of vitamin C is a possible factor in failure of wound healing, particularly in patients with a long and continued avitaminosis. Their observations cast some doubt on the role of ascorbic acid in the production of anemia, however.

Extent of Vitamin Deficiency

There is at present considerable disagreement about the extent of malnutrition in the United States. On the one side of the question, one finds the clinical experience of Alvarez[129] and others that gross disease due to avitaminosis is not often recognized in highly reputable clinics. In his inimitable manner, Clendening[130] has presented this side of the case, addressed particularly to readers who have a sense of humor. On the other side, one finds the estimate by Parran[131] that 45,000,000

people in this country do not enjoy optimal vitamin nutrition. This figure is based on the careful study of four thousand American dietaries by Stiebeling and Phipard.[132]

The problem boils down to what has been called "hidden hunger," which, by definition, cannot be diagnosed clinically. How important this state may be in the daily lives of the apparently healthy or of the obviously ill can be answered only when careful functional studies, physiologic and psychologic, are correlated with carefully measured vitamin metabolism. Such a study, indeed, is now in progress at the Lockheed Aviation Plant in Los Angeles as part of a program recommended by the Committee on Nutrition in Industry of the National Research Council.

In the meantime, chemical studies can be applied in the routine clinic to ascertain how great a factor of safety has been afforded by the diet in the individual case. Until it is clear how low a saturation can be tolerated, obviously the safest policy is to ensure liberal replenishment of vitamin stores. In chronic illnesses accompanied by restriction of food, whether spontaneous or enforced, mild vitamin deficiency may lurk unsuspected in the background as a contributory element in the total discomfiture of the patient.

Such data must, of course, be correlated with parallel clinical observations. For example, examination with the slit lamp[133] may be utilized to detect characteristic changes in the corneas of patients deficient in vitamin B_2, or to detect Bitot spots[134, 135] due to lack of vitamin A. Likewise, the study of other chemical substances, such as pyruvic acid metabolism in vitamin B_1 deficiency, may give specific evidence of disturbed nutrition.[136] At the present time, there is need of many such collateral data before final conclusions can be drawn. Eventually, however, chemical data will afford a convenient parameter by which to integrate many facts drawn from diverse sources.[137] Indeed, Mason and Williams[138] have recently emphasized the utility of such a procedure in clinical studies of thiamin deficiency. This will be particularly valuable in cases of conditioned deficiency, when the nature of the dietary offers little clue to the nutritional status of the patient.

* * *

It may be recalled that convenient methods are available for determining the concentration of the commonly known vitamins in the blood and excreta of human subjects. The use of these procedures has been extended to various types of tolerance and saturation tests. These serve to estimate the extent of tissue stores of vitamin and the avidity with which body tissues retain vitamin. In general, studies of urinary excretion are probably more significant than the analysis of blood, except in investigations of vitamin A.

The interpretation of the results obtained by these tests requires further statistical study. How impoverished in vitamin must a patient be before he is considered unhealthy? Obviously, a biochemical method cannot answer this question, but it can at least measure the degree of vitamin lack. Already, there is considerable evidence that in Minot's "twilight zone" of subclinical vitamin lack, human efficiency and effectiveness may be greatly impaired. In the impending strain on national resources, this approach will assume particular importance.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28171

PRESENTATION OF CASE

A seventy-year-old Irish-American was admitted to the hospital because of tarry stools.

About thirteen months before entry, the patient noticed that his stools frequently included small amounts of bright-red blood or streaks of dark blood, or occasionally were frankly tarry. Bowel movements continued regular, without resort to cathartics. There was no pain or distention. The patient visited the clinic of another hospital and had a roentgenologic examination of the gastrointestinal tract that was said to be negative; the symptoms continued, as before. A week before entry, he consulted the clinic of this hospital and was proctoscoped, with visualization of small, high internal hemorrhoids. A roentgenogram of the colon showed an irregular narrowing of the lumen of the midsigmoid, over a distance of 6 cm. The proximal end showed a "slightly intussuscepting" filling defect. The mucosal pattern in this area was abnormal. There were several diverticula of the sigmoid and lower descending colon. The remainder of the colon, the appendix and the terminal ileum appeared normal.

Two sisters of the patient had died of tuberculosis. When he was between twenty and thirty years old, the patient had several "nervous breakdowns" characterized by personality disturbances and dipsomania. For many years after this, he experienced occasional nausea and vomiting after breakfast. Five years before entry, he had hemorrhoids removed at another hospital. Three years later, after a period of urinary frequency terminating in an episode of acute retention, the patient had a two-stage prostatectomy, also in the other hospital. At about this time, he developed an eruption on the left cheek. A year later, he consulted the clinic of this hospital. Biopsy of the lesion, three months before entry, showed carcinoma of undetermined type. In the following month, 4300 r of roentgen therapy was given to the cheek, with resultant regression of the lesion.

On admission, the patient appeared well preserved, plethoric and in good health. A mottled scar, 2 cm. in diameter, lay on the left midcheek. The heart and lungs were essentially normal. The abdomen was soft, with an elongated mass in the left lower quadrant that could be rolled between the examiner's fingers. There were no other palpable masses. There was a small hernia at the site of a midline suprapubic old operative incision, and a right direct inguinal hernia. Rectal examination was negative.

The blood pressure was 240 systolic, 120 diastolic. The pulse, temperature and respirations were normal.

Examination of the blood showed a red-cell count of 4,900,000 with 90 per cent hemoglobin, and a white-cell count of 7800 with 66 per cent polymorphonuclears. The urine was normal.

A roentgenogram of the chest showed only tortuosity of the aorta, and old calcified tuberculous foci in both upper lobes. An electrocardiogram showed changes consistent with either hypertensive or coronary heart disease.

On the third hospital day, cecostomy and appendectomy were performed under local anesthesia. There was little postoperative reaction, and the cecostomy tube drained well. A roentgenogram of the large bowel showed marked delay in passage of barium above the abnormal area noted in the previous examination.

On the fourteenth hospital day, a second operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD L. YOUNG: This is a case in which we must discuss the differential diagnosis of a tumor of the midsigmoid causing partial obstruction. The possible causes are many, the probable causes few. This patient had a fairly normal bowel habit, no changes being apparent in the stools except for the presence of blood, so that we can almost surely throw out any ulcerative form of colitis. The things that must be considered in the order of probability are: cancer and diverticulitis, infectious granulomas and the rare tumors, such as sarcoma or some form of benign tumor, such as lipoma. Also, we might consider intussusception as a mere possibility. Although chronic intussusception does exist, it is generally of the ileocolic variety, it is very rare at this age, and its presence does not cause bright blood, so that I think we can discard that diagnosis. Tuberculosis is a possibility. To make us consider tuberculosis is the fact that the x-ray examination showed old tuberculosis in the patient's lung. Tuberculosis of the bowel is usually a disease of young people. Furthermore, tuberculosis usually involves the ileocolic region, and is generally, though not necessarily, accompanied by a certain degree of activity of the pulmonary tuberculosis. In this case, the disease was on the left; it was not the ulcerative but the hyperplastic type because of the tumor

felt. I believe that we can discard tuberculosis. Because of their rarity, we need not consider infectious granulomas of other origin.

The case boils down, then, to a differential diagnosis between carcinoma and diverticulitis, both of which could fit the picture. We used to be taught that patients with diverticulitis rarely bled and that when either gross or microscopic blood was present we should always look for some other disease. However, we now believe that at least 20 per cent of the patients with diverticulitis do bleed at some time or other, although it is not common to have so much bleeding as this patient had. Moreover, a subacute perforation with an infectious area about the bowel could cause such a tumor as that felt in this case, and we do know that diverticula were visible on the x-ray films. Carcinoma, of course, can fit this picture very well. We must remember, moreover, that both could exist in the same case. I believe, however, that when this is so there is no connection between the two. Is it possible, then, to differentiate these two lesions? I think that the x-ray films are the best evidence we have, and I should rely largely on what the radiologist says. If the statement "slightly intussuscepting" means anything, it certainly suggests a proliferative type of growth of the inside of the bowel. What about it, Dr. Hampton?

Dr. Aubrey O. Hampton: I think the report reads a little more obviously like tumor than the films do. In the large one, practically everything is obscured by what appears to be diverticulitis, and there is a good deal of spasm in the sigmoid. This second film must be the one from which they concluded that the mucosa was abnormal. The area of involvement is only about 3 or 4 cm. I think this may be what they meant by the intussuscepting defect, but I do not believe that we have any evidence of intussusception. We have evidence of diverticulitis and absence of mucosa over a distance of 4 cm., with an apparent filling defect.

Dr. Young: Should you be willing to make a diagnosis on the x-ray films as they stand?

Dr. Hampton: I think I should, with a little reservation.

Dr. Young: If we may believe that diagnosis, what is the treatment? With the two in our mind, the main thing to do is treat it as cancer because I do not believe the surgeon exists who can feel of this with his hand in the abdomen and be sure which it is. Therefore, it must be treated as a cancer. In this seventy-year-old man, the blood pressure was 240, and the justification of any operation is that the hazard of operation, in the last analysis, is no greater than that of the condition one is operating for; the outcome, if the condition is cancer, is certain death. So that one is justified in going the distance. I believe the evidence points more strongly to cancer than to diverticulitis.

Dr. Reed Harwood: Did the laboratory test show occult blood in the stools?

Dr. Tracy B. Mallory: Yes; on the single specimen examined.

Dr. Chester M. Jones: It certainly is most unusual to have that much blood from diverticulitis, although one does see some blood occasionally.

Dr. Mallory: One interesting sidelight is that during the entire period covered by this story, the patient was being treated in our tumor clinic for carcinoma of the cheek. He never told anyone in this hospital, however, about the abnormality of his stools. He went to another hospital with that story, and the first x-ray examinations were done there and were negative.

Dr. Young: Do you mean that they did not spot the diverticula?

Dr. Mallory: So the report says. It is hard to believe.

Dr. Hampton: I do not believe that they missed them.

Dr. Harwood: It seems unusual to have a normal red-cell count and hemoglobin with bleeding for thirteen months.

Dr. Claude E. Welch: The patient was not the most intelligent Irishman I have seen, and we doubted much of the story. There is no question that he bled a good deal, however. We thought he had carcinoma of the colon on the basis of the first x-ray report. But, in view of the visible diverticula, we had enough doubt about the situation to do a second barium enema, twelve days after the first, to determine whether there had been any change. The report that came back from that was "absolutely no change," and we justifiably thought that we had additional evidence in favor of the existence of two lesions—diverticulitis and carcinoma. At the time of the second operation, it was noticed that the patient had a tremendous mass of adhesions in the lower pelvis, large enough for us to be tempted to say that the lesion was inoperable. With a little difficulty, the lesion was resected, and anastomosis done. The patient had a perfectly uneventful postoperative course.

Dr. Hampton: The way the case is building up, I am sure that Dr. Young and I will be wrong. The films, however, certainly suggest that the patient had a carcinoma.

Dr. Young: I was going to ask if you would "stick your neck out" too.

Dr. Hampton: I looked at all the films and did not think of it until I saw the last spot film,

which looks very much like carcinoma. The other films look like diverticulitis.

DR. YOUNG: The question of whether the mucosal layer was gone is important, and I assumed you said it was.

DR. HAMPTON: It appeared to be. I cannot be certain. One can have edema or constriction from outside pressure or infection, and the mucosa will appear to be abnormal.

DR. YOUNG: Did you feel the mass at the time of the first operation?

DR. WELCH: No attempt was made to palpate it at the time of cecostomy.

CLINICAL DIAGNOSIS

Carcinoma of sigmoid.

DR. YOUNG'S DIAGNOSIS

Carcinoma of sigmoid.

ANATOMICAL DIAGNOSIS

Diverticulitis of sigmoid.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The resected specimen showed multiple diverticula, several of which were inflamed. There was no evidence of tumor. The mucosa between the diverticula was markedly edematous, producing a pseudo-polypoid appearance, which accounts for the abnormal mucosal pattern in the films.

DR. HAMPTON: Was there an abscess?

DR. MALLORY: No frank abscess.

DR. HAMPTON: No perforation?

DR. WELCH: No.

CASE 28172

PRESENTATION OF CASE

First admission. A fifty-six-year-old housewife was admitted to the hospital because of cramping lower abdominal pain and vomiting.

The patient had been constipated for many years and on occasion used various laxatives, but she had no pain or other symptoms referable to the bowels. Three days before entry, following an upper respiratory infection of several days' duration, there was a fairly sudden onset of severe cramping pain, extending across the lower abdomen from the right lower quadrant. The patient took a proprietary laxative and vomited almost immediately. Several additional doses of the medicine were then taken, with subsequent partial abatement of the cramps. On the day preceding admission, there was further vomiting, and the cramping became severer despite further doses of laxatives and hot rum punch. On the first day of the illness, the patient had two or three bowel movements, on the second day one or two, on the third day four, and on the day of admission none. None of the movements included evident blood.

Six years before entry, the patient had a complete hysterectomy, a bilateral salpingo-oophorectomy and an appendectomy performed at another hospital, with the finding of leiomyomas of the uterus, chronic cervicitis and bilateral early cystadenomas of the ovaries. Four years later, mastectomy was performed in the same hospital, in treatment of a benign intraductile papilloma. The next year, the patient had a sacral laminectomy at this hospital because of backache and swelling over the lower spine. Two paradural cysts of unknown type were drained, but not removed or biopsied. Aside from these difficulties, the patient was in good health.

On admission, the patient appeared well nourished but acutely ill, with flushed face, dry, coated tongue and warm skin. The nose and throat were mildly injected. The lungs were clear. The heart was normal. The abdomen was distended, with hypoactive peristalsis. An area of erythema over the left lower quadrant suggested a burn from a hot-water bottle. There was generalized abdominal tenderness, most marked in the left lower quadrant, where voluntary rigidity was also most marked. There was rebound tenderness all over the abdomen, which was referred to the point in the left lower quadrant that was most tender on direct pressure. Pelvic examination showed boggy induration of all sides of the vagina, without definite masses. Tenderness was somewhat more marked on the left. Rectal examination showed induration high on the anterior wall of the rectum.

The blood pressure was 140 systolic, 80 diastolic. The temperature was 103°F., the pulse 100, and the respirations 20.

Examination of the blood showed a white-cell count of 15,050, with 80 per cent hemoglobin. The urine was normal. The blood chemical findings were essentially normal.

On the fifteenth hospital day, a roentgenogram of the large bowel showed prompt filling of the rectum and distal sigmoid. At the junction of the middle and proximal thirds of the sigmoid, there was a more or less annular area of narrowing, conical in its distal portion, causing almost complete obstruction. There was no definite edge to this lesion, suggesting an extrinsic pressure defect. A small pouch just above the area of narrowing was consistent with a small diverticulum.

On the twenty-fourth hospital day, a Devine colostomy was performed. Exploration of the abdomen showed a mass in the pelvis apparently

continuous with the sigmoid, which felt irregular, edematous and fixed. Adhesions were present in the region of the old laparotomy scar. There was no evidence anywhere of metastatic disease. Following operation, there was some fever, which slowly subsided. The patient was discharged on the twenty-fourth postoperative day, with the colostomy working well.

Second admission (eleven months later). The patient continued well, following discharge. There was no pain, fever, cramping or rectal bleeding. A follow-up roentgenogram showed obstruction of the sigmoid, quite similar to that noted in the previous examination. Barium introduced through the colostomy opening into the distal segment of the colon passed readily to the area of obstruction, outlining a few small diverticula just proximal to the obstruction.

On re-entry, physical examination was essentially as before, except that the abdomen was free from tenderness and distention. The rectum admitted a proctoscope to a distance of only 13 cm., owing to angulation of the bowel. The mucosa appeared edematous, injected and friable.

Examination of the blood showed a white-cell count of 8800. The blood chemical findings were normal.

An intravenous pyelogram was negative.

On the fifth hospital day, an operation was performed.

Differential Diagnosis

Dr. Henry H. Faxon: I can save considerable time by referring to the discussion that Dr. Young has just given. Here, again, we have a differential diagnosis of a lesion in the sigmoid with the same possibilities that he has already mentioned. Before I heard the final outcome of his problem, I had planned to emphasize what Dr. Jones has said: that bleeding is most uncommon with diverticulitis. On the basis of the bleeding in the preceding case, I should have been extremely skeptical that the lesion was due to diverticulitis.

My discussion of this case is based on the same premise that the absence of gross blood is suggestive of a diagnosis of diverticulitis. The disease that the patient apparently now has is obviously in the sigmoid. The outstanding points, it seems to me, are that the two acute episodes were of short duration, that especially the first of these was marked by the manifestations of infection with an elevated temperature and so forth, and that nearly a year elapsed between the two hospital entries. Let us see now if the X-ray Department can help us.

Dr. Aubrey O. Hampton: The picture suggests something surrounding the bowel at the point of maximum narrowing. I believe that the mucosal folds are intact. They could be absent on one side, but I shall stick to the record that the lesion was probably extrinsic and that a diverticulum was present.

Dr. Faxon: A possible undetected endometriosis affords the only connection between the present lesion and that for which the previous hysterectomy was done. It is not uncommon to find the large bowel involved in endometriosis, but since the ovaries had been taken out at the time of the operation six years previously, it would be surprising if endometriosis played any part in the present involvement of the large bowel. We have definite information from the operative note that seems to exclude cancer. If a malignant lesion was present, it was at any rate unrecognized by the operator. Furthermore, eleven months went by before the patient again appeared with the same symptomatology and the same type of picture.

What the operation for paradural cyst was and what significance can be attached to it, I frankly do not know. I do not believe that it played a part in the present bowel disease, but I may be overlooking a good lead in merely dismissing it.

I believe that one of the diverticula actually ruptured and gave rise to infection about the bowel, and that with the sidetracking afforded by the Devine colostomy the inflammation quieted down. Many such inflammatory masses are hard to distinguish from cancer at operation, as Dr. Young has said. They often subside but, if due to diverticulitis, often recur in similar fashion. I believe that the primary lesion in this case was diverticulitis.

Dr. Hampton: What was the X-ray Department's conclusion?

Dr. Tracy B. Mallory: They did not say anything more than "inflammatory mass." It is probably safe to assume that they were thinking of diverticulitis.

Dr. Hampton: That is the implication I meant to leave.

Dr. Claude E. Welch: Is that not very unusual for that length of time?

Dr. Hampton: It seems that diverticulitis should have improved more than this patient's had.

Dr. Welch: Especially with colostomy.

Dr. Hampton: And especially since, at the first examination, the bowel looked somewhat flexible. It did not look like the chronic scarring of diverticulitis.

Dr. Howard Ulfelder: I performed the first operation in this hospital, and of course responsibility for diagnosis could not rest on that procedure.

It was done merely to defunction the large bowel. I thought I overstepped myself at the time in exploring the patient as much as I did, in view of the very recent pelvic sepsis. However, I did exclude cancer to the best of my ability. I found a well-fixed mass in the pelvis and a normal liver, and then did a transverse colostomy.

Clinical Diagnosis

Diverticulitis of sigmoid.

Dr. Faxon's Diagnosis

Diverticulitis of sigmoid.

Anatomical Diagnoses

Carcinoma of sigmoid.
Chronic inflammation, with abscess formation in mesentery.

Pathological Discussion

Dr. Mallory: At the second operation, the findings were quite different. At that time, it was obvious that the pelvis was quite well filled with carcinoma. It was also clear that the disease was incurable; however, it was decided that enough relief of symptoms could be obtained by resection to justify such a procedure. There was an inflammatory mass in the mesentery, and to a considerable extent the conclusions of the radiologist were justified; but it was a carcinoma, not a diverticulum that had undergone a subacute perforation.

Dr. Hampton: How big was the carcinoma?

Dr. Mallory: It was an annular lesion about 3 cm. in diameter.

Dr. Hampton: I cannot find it in the x-ray films.

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MALPRACTICE INSURANCE FOR PHYSICIANS IN MILITARY SERVICE

A letter in this issue of the *Journal* brings up the question whether a physician in military service should carry malpractice insurance.

In an editorial, "Malpractice Actions against Army Medical Officers and Examining Physicians for Local Selective Service Boards," in the September 13, 1941, issue of the *Journal of the American Medical Association*, it was stated that the Judge Advocate General of the United States Army had ruled, on May 1, 1941, that members or prospective members of the Army are entitled to the same civil rights of action between one another with reference to suits for malpractice or negligence as they would have in civil life. Hence, a man in military service who has been attended by a medical officer in line of duty or a selectee who has been examined by a physician attached, either in a civilian or military capacity, to a selective-service or induction board may bring suit for alleged malpractice. Although no official statement has been offered by the Judge Advocate General of the United States Navy, it seems likely that the same ruling would be made. Furthermore, several of the commercial companies that offer malpractice insurance have recently announced a new type of policy, which covers physicians who are in military service.

Whether this type of insurance is necessary is a matter that each medical officer must decide. It is obvious that all physicians who serve in a civilian capacity on selective-service or induction boards are protected against malpractice suits if they carry standard policies, — and if they are not insured, they are running no more risk than they do in everyday practice. In addition, the chance that suit will be brought by a man in active military service is exceedingly unlikely, — as shown by the relatively low rate of the military policy, — and if action is taken, it has been the custom to transfer the case to a federal court and to furnish the defendant with federal counsel designated by the Department of Justice. In spite of the fact that there is, at present, no legal provision for the Government to pay the claim or to reimburse the defendant if a judgment favorable to the plaintiff is rendered, at least one branch of the service — the Selective Service System — has intimated that it would make an attempt to protect him from financial loss, even if this required a special act of Congress. Although the possibility of personal loss by a well-trained medical officer seems extremely unlikely, the risk does exist and should probably be covered by a military policy.

THE KENNY METHOD OF TREATMENT OF INFANTILE PARALYSIS

Miss Elizabeth Kenny, a nurse from the hinterland of Australia, developed a treatment for poliomyelitis that is now being widely used in this country. She has carried on her work in America

under the auspices of the National Foundation for Infantile Paralysis, having demonstrated her method before a qualified group of observers at the University of Minnesota. The reports now available suggest that the results of her treatment of patients both in the acute and in the chronic stage of poliomyelitis are unusually satisfactory. In many cases, she has prevented the development of contractures and deformities, and in general, the muscles of these patients have shown less than the usual amount of paralysis. In other words, most observers who have visited the clinic established in Minneapolis have come away impressed by the results obtained. In view of the success of her treatment, plans are being made to publish the essential facts, as well as a discussion of Miss Kenny's ideas, in a pamphlet to be issued by the National Foundation for Infantile Paralysis. Until this is available, those who are interested should consult Miss Kenny's book.*

Her account, however, is difficult to understand, since many of her arguments require definitions of the terms that she uses. For instance, the word "spasm" is used in a manner foreign to current medical understanding. She speaks of spasm as a primary symptom of paralysis, and considers fibrillation, twitching, hyperirritability to stretching and a tonic state of contraction to be signs of spasm. She believes that spasm is responsible for the paralysis and also for the malposition of the limbs. Flaccid paralysis as a primary symptom of the disease is denied by Miss Kenny; she contends that muscles cannot move, not because they are paralyzed, but because they are overstretched by the opposing group of muscles in spasm. Miss Kenny uses two other confusing terms, "inco-ordination" and "mental alienation." Inco-ordination, according to the interpretation, depends on muscle spasm and is the result of the spreading of impulses to other muscles because the muscle involved exhibits pain or is unable to move. Inco-ordination may also be caused by ineffective contractions in the affected muscles. Mental alienation, the third term, deals with the inability of muscles to function because of the spasm and pain due to the contraction of opposing groups or because of the interruption of pathways from processes in the central nervous system not permanently destroyed. These three terms, as will readily be appreciated, are almost foreign to medicine, and without Miss Kenny's definitions of them, one cannot even attempt to understand her method and reasoning.

Whatever the theoretical considerations concerning Miss Kenny's work, there can be little doubt of the practical value of her treatment. Although not particularly easy to understand or simple to carry out, the method can be learned in a year by any well-trained physician or physiotherapist. It consists essentially of continuous attention from a highly trained staff of attendants, with the absence of manipulation, all appliances or any form of treatment that will increase the spasm in the affected muscles. Massage in all forms should be avoided. Pressure from the bedclothes, unnecessary handling and pressure from casts and splints, according to Miss Kenny, increase spasm. The spasm itself is treated by hot fomentations applied in a careful and routine manner. Moreover, she does not believe in the testing of muscle strength in acute poliomyelitis, since these determinations tend to increase spasm and pain and therefore to retard recovery. When pain and spasm have been overcome by hot fomentations, active therapy is started. The technics of muscle re-education developed by Miss Kenny call for an intimate knowledge of muscle anatomy and function. Thus, the excellent end results seen in her cases are brought about through careful treatment by use of physiotherapy of a specialized nature directed toward inco-ordination and alienation, as well as through the proper application of heat during the stage of spasm.

The Kenny method completely revolutionizes modern ideas regarding the treatment of acute poliomyelitis. Muscle testing, splinting, avoidance of overstretching, absolute rest and many other procedures are largely overthrown, and additional modifications will naturally follow.

*Kenny, E. *The Treatment of Infantile Paralysis in the Acute Stage.* 285 pp. Minneapolis and St. Paul: Bruce Publishing Company, 1941.

If the technic is adopted, the physician, whether he is a pediatrician, orthopedist, neurologist or clinician, must begin treatment of the affected muscles on the very first day of the disease: in most cases this means starting intensive therapy in a hospital for infectious diseases. Furthermore, treatment must be continued unremittingly until all power that is possible returns to the affected muscles.

MEDICAL EPONYM

Oppenheim's Sign

Hermann Oppenheim (1858–1919), of Berlin, presented a discussion, "Zur Pathologie der Hautreflexe an den unteren Extremitäten [On the Pathology of the Skin Reflexes in the Lower Extremities]," in the *Monatsschrift für Psychiatrie und Neurologie* (12: 421–423, 1902). A portion of the translation follows:

> If the handle of the percussion hammer is drawn down along the inner aspect of the lower leg (about at the posterior margin of the tibia or even beyond it) in healthy persons, there will be seen either no motion of the foot and toes, or a plantar flexion. . . . In patients presenting the symptom complex of spastic paraplegia or hemiplegia, the maneuver described usually results in a reflex muscular contraction causing an extension of the great toe, and either adduction or abduction of the foot.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Case History: Hydramnios followed by post-partum hemorrhage, hysterectomy and death

A thirty-seven-year-old essential primipara (there had been one spontaneous abortion) who had had excellent prenatal care developed an upper respiratory infection for which she was hospitalized at the very end of her pregnancy. There undoubtedly was some mistake concerning dates, since the record states that labor did not set in until five weeks after the estimated date. There had been no complications during pregnancy; the blood pressure and urine were normal, and the past history was irrelevant. A diagnosis of hydramnios and anencephalus was made before labor. Although it is not so stated, an x-ray film had in all probability been taken on which this diagnosis was based. The upper respiratory infection was not accompanied by fever. Labor started spontaneously by the rupture of the membranes, and eighteen hours later the patient was delivered normally, with the aid of cleidotomy. The weight of the baby is not given, but presumably it was a large child. A second-degree tear of the perineum was sustained and immediately repaired. The placenta, delivered normally, was followed by tremendous hemorrhage, and the uterus was packed. The patient was given four transfusions. Since the uterus continued to bleed, an abdominal suprapubic hysterectomy was performed eight hours after delivery. In spite of three additional transfusions, death occurred ten hours later. No autopsy was performed.

Comment. Hydramnios, with the resulting overstretching of the uterus, has always been considered a possible cause of post-partum hemorrhage. For the same reason, the stretching that accompanies twin pregnancies may also result in bleeding. In all such cases, the fundus should be very carefully watched after delivery; sometimes, the intravenous use of ergotrate is of value in combating atony. All that could possibly have been done for this patient was done. The fatality merely emphasizes the occasional seriousness of post-partum hemorrhage and the ever-present possibility of the need for hysterectomy and for repeated transfusions.

DEATHS

CRANE — Clarence Crane, M.D., formerly of Boston, died April 13. He was in his seventy-second year.

Born in Salem, Oregon, Dr. Crane received his degree from Boston University School of Medicine in 1900. He was assistant professor of surgery at Boston University School of Medicine from 1900 to 1921, and staff surgeon of the Massachusetts Memorial Hospitals. He was a former member of the Massachusetts Medical Society and the American Medical Association, and a fellow of the American College of Surgeons.

He is survived by his widow, three sons, and two daughters.

PERRY — Sherman Perry, M.D., of Winchendon, died April 20. He was in his sixty-fourth year.

A native of Passaic, New Jersey, Dr. Perry received his degree from Harvard Medical School in 1907. He served on the staffs of the Worcester City, Boston Children's and Tewksbury State hospitals and was a former president of the Worcester District Medical Society. He was a member of the New England Obstetrical and Gynecological Society, and a fellow of the American Medical Association.

His widow survives him.

WALKER — John B. Walker, M.D., formerly of Boston, died April 13. He was in his eighty-third year.

Dr. Walker received his degree from Harvard Medical School in 1888. He was formerly on the staff of the Boston City Hospital and was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, two sons and two daughters.

WAR ACTIVITIES

CIVILIAN DEFENSE

Hospitals To Be Reimbursed for Care of Civilian Casualties

Payment for temporary hospitalization of civilians injured as the result of enemy action has been made possible by a recent agreement between Administrator Paul V. McNutt of the Federal Security Agency and Director James M. Landis of the Office of Civilian Defense. The funds have been allocated to the United States Public Health Service by the Federal Security Administrator from sums made available to him from the President's emergency fund. A joint memorandum embodying the details of the program has been issued by Surgeon General Thomas Parran of the United States Public Health Service and Dr. George Baehr, chief medical officer of the Office of Civilian Defense.

The plan provides that all hospitals caring for civilian casualties in the event of air raids or other enemy action will be reimbursed by the federal government at a rate of $3.75 a day. This is the rate of reimbursement established by the Federal Board of Hospitalization for federal beneficiaries in government hospitals and may be changed as conditions require, it was stated.

Any hospital in the Nation, voluntary or governmental, may be used as a casualty receiving hospital in the Emergency Medical Service established by the Medical Division of the Office of Civilian Defense. In addition, certain hospitals and other institutions in "safe areas" may be used as emergency base hospitals for casualties or other patients whom it may be necessary to evacuate from urban hospitals in exposed areas. The new agreement provides that federally owned equipment may be loaned to the base hospitals and that their staffs will be supplemented by physicians of the region who will be commissioned in the reserve corps of the United States Public Health Service. It was emphasized that management and control of all hospitals, both local casualty-receiving hospitals and emergency base hospitals, will remain the responsibility of the local or state authorities.

In the establishment of emergency base hospitals, emphasis will be placed on the relative safety of the area and the availability of existing hospitals and other institutions. Hospitals are now being surveyed for this purpose and will be classified on a basis of size, equipment and standards of operation.

It is proposed to begin immediately the organization of medical staffs for future base hospitals as hospital units affiliated with casualty hospitals similar to the affiliated general hospitals of the Army. The physicians, surgeons, specialists and dentists who are to be commissioned in the Public Health Service Reserve for service in these hospitals will receive rank, pay and allowance equivalent to those of the Medical Corps of the United States Army. They will be selected from older age groups, from physicians with disabilities that make them ineligible for military service and from women physicians. So far as possible, they will be assigned to service in the regions in which they live. Because they are to function as balanced professional staffs, they will be recruited from the staffs of civilian hospitals and cleared through the Procurement and Assignment Service.

MISCELLANY

"TUBERCULOSIS IS FOUND WHEN LOOKED FOR"

The gap between proved knowledge and effective action based on that knowledge is nowhere more glaring than in our fumbling efforts at control of the commonest of the infectious diseases.

We know that the time lost from the common cold would build hundreds of the planes we now need so much. Yet, the simple prophylactic measure of isolating all those with colds in early stages is applied routinely to a few school children only.

This failure to co-ordinate knowledge and action is also all too common in our efforts to control and eradicate tuberculosis.

That tuberculosis can be found and is most easily cured in the stage before symptoms appear is an axiom that has grown trite with repetition, yet the great majority of people fail to translate this into the action that will safeguard themselves and their families from this disease.

But what are the facts? In four years, the deaths from tuberculosis surpass the number of those killed in all the wars the United States has ever fought. If the losses of one year from tuberculosis could be attributed to enemy action, the nation would be shocked with grief and vow vengeance at any cost. Yet the slow undramatic dribbling away of lives goes on, day by day, although proof has been added to proof that this can be stopped.

An example is provided by colleges and universities. Into their doors every fall go hundreds of thousands of American youth, those favored ones of earth from whose ranks come most of the trained men and women of our society. Yet tuberculosis has already laid its hand on many of these. During 1939–40, according to the report of the Tuberculosis Committee of the American Student Health Association, published in the *Journal-Lancet*, 637 cases of tuberculosis were found in two hundred and forty-eight of these institutions with a total enrollment of 500,000 students, because it was looked for. Most of these infected students can be saved for useful, productive lives with a minimum of time lost.

What is the story where the college authorities report that no search is made? The fact that only 35 cases appeared in two hundred and twenty-seven institutions among 200,000 students during the same period provides the answer. But is that the whole story? No; for back of those 35 cases many more stand in shadowed ranks, already touched by the destroyer. It is easy to prove that tuberculosis is there — a tuberculin test, followed by an x-ray film of positive reactors, is the magic wand that will bring to light the hidden lesions. But when they are not found early, we know the story too. Most of them progress to the stage where treatment is to be reckoned in years, and complete cure is the exception.

And what of the four hundred and two institutions whose administrators did not even reply to the questionnaire? One can only surmise that they, too, have failed to translate the thing they know into the thing they do. Some of them, perhaps, are even unaware that tuberculosis is now, as it has always been, a foe of youth.

Yet it is to the pursuit of knowledge that all these institutions are dedicated, and it was many years ago that Ralph Waldo Emerson said: "Education is not pouring knowledge into minds; it is not erudition. A person is not truly educated unless knowledge influences his

doing as well as his *thinking*. Insofar as learning alters and directs *behavior* it is education."

In this respect, unfortunately, educators follow but the common path. In the trade union, the insurance office and the department store, in the hospitals and the homes for the aged, wherever men and women are gathered together, tuberculosis may be found when looked for. No class is exempt; no land is free from it — it is an enemy power we know how to conquer, but the war is prolonged by "too little and too late." — Reprinted from *Tuberculosis Abstracts*, April, 1942.

CORRESPONDENCE

MILITARY MALPRACTICE INSURANCE

To the Editor: I wish to call to the attention of all physicians entering the armed services of the United States or serving as examining physicians for local selective-service boards that they may be sued by selectees, or by anyone in the armed services of the United States, treated by the medical officer, on an allegation of malpractice. This ruling, dated May 1, 1941, was made by the Judge Advocate General of the United States Army.

Military policies, available on and after April 10, 1942, provide $2500 to $7500 limits for $10.00 a year. These policies are issued by the insurance companies solely for malpractice insurance covering physicians in military service. If any income is derived by the medical officer on active military service from association or agreement with a physician in private civilian practice, the military policy does not apply. If a medical officer desires a military policy, he must certify that he was a member of his state medical society or association when inducted into the service.

Medical officers discharged from the armed services and entering practice again should remember to reinstate their regular malpractice insurance policies for protection in civil life, if they desire such protection.

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REPORTS OF MEETINGS

NEW ENGLAND PATHOLOGICAL SOCIETY

A regular meeting of the New England Pathological Society was held on November 20, 1941, with Dr. B. Earle Clark presiding. Dr. William Dock, professor of pathology at Cornell Medical College, spoke on "The Kidneys and Hypertension."

Scarring or compression of the kidneys and partial occlusion of the renal artery or of the aorta proximal to the renal artery leads to sustained hypertension, and since this persists for hours after removal of the kidney it cannot be due to a reflex; it might be caused by decreased liberation of an antipressor substance or release of a pressor hormone, which seems likelier, since total nephrectomy does not cause a rise in pressure. All attempts to demonstrate a vasoconstrictor substance in renal hypertension have failed; indirect evidence from studies of flow in the limbs does not prove that such a substance is present in human patients and rules it out in the transient hypertension of acute glomerulonephritis (Pickering). Dr. Dock and his collaborators have found no difference in the pressure levels of control and renal hypertensive rats, rabbits and dogs, after destroying the central nervous system. Pithed animals are very sensitive to vasoconstrictor substances, including renin, and it is therefore concluded that the renal pressor hormone acts by changing the set of the vasomotor center, and not directly on arterioles.

Perfusion of kidneys post mortem and x-ray films of the injected renal arterial bed prove that an organic increase in resistance to renal blood flow is not usual in hypertensive patients without uremia; narrowing of the main artery is even rarer. In most cases, the kidney shows, in addition to atheromatous narrowings, arteriolar change equal to that in the other kidney, whereas in Goldblatt-clamp hypertension, little or no change is present in the kidney protected by the clamp even though marked change occurs in the retinal vessels and in the opposite unprotected kidney. Accordingly, Dr. Dock considers most narrowed main renal arteries to represent late complications, not primary causes. There is strong evidence, based on the evolution of vascular disease in the eyegrounds and on studies of Goldblatt hypertension and pulmonary arterial sclerosis, that hypertension may cause or accelerate atherosclerosis and arteriolar degeneration. Therefore, it is most probable that renal sclerosis is a result, not a primary cause, of so-called "benign" hypertension. At present, it seems probable that inherent vasomotor instability or adrenocortical disease underlies many cases of arterial hypertension, and that the tendency to vascular degeneration inherited by some people leads to rapid renal, retinal, cerebral or coronary arterial disease if they become hypertensive. Others, especially women, have inherent soundness of the vascular tree, and after decades of hypertension show minimal damage.

Rodents, dogs, cats and men have easily recognized peculiarities of the first loop of the distal convoluted tubule (macula densa) and of the wall of the afferent arteriole. No definite change in this tissue is seen in most human hypertensive patients (benign, glomerulonephritic or pyelonephritic coarctation of aorta), or in rats, rabbits and dogs in which hypertension has developed slowly and gradually; changes have been seen by others in many types of renal hypertension in animals, and Dr. Dock has observed hyperplasia and swelling of the cells of the afferent arteriole in dogs with rapidly developing hypertension and has been much struck by the hypertrophy and fuchsinophilic granules in the arterioles of the hypertensive cat (Graef). He has also been struck by the severe damage to this tissue in amyloid disease, and suggests that the absence of hypertension in most amyloid uremic cases is due to the fact that the specific cells have been replaced by amyloid. However, it must be noted that uremia in amyloidosis often develops rapidly and may be due to an extremely severe damage to the adrenal cortex. Dr. Dock found excellent renal perfusibility in one case of amyloid disease with uremia. Careful study of amyloidosis, with and without hypertension and during life as well as post mortem, may prove valuable in correct judgment of the role of the juxtaglomerular tissue. The morphologist, whose observations usually start most clinical problems, may be able by refined technics in pedigreed cases to solve a complicated situation.

In the discussion, neither Dr. Soma Weiss nor Dr. Alan Moritz considered the evidence presented by the speaker sufficient to rule out the renal origin of hypertension. Dr. Weiss believed that the evidence drawn from the pithed-animal experiments was not foolproof, since it is known that vasoconstrictor substances may act differently under various conditions. Dr. Moritz stated that the possible causal relation of renal arteriolar disease and hypertension is still an open question.

HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on December 9, with Dr. Soma Weiss presiding.

The case presentation was that of a forty-one-year-old woman whose history dated from an attack of acute otitis media eleven months prior to admission. There were recurrent episodes of draining from the ears for three months, followed by a period of one month without symptoms. Then began a train of manifestations including fever, chills and night sweats. Four blood cultures were found to be positive for *Streptococcus viridans*. Sulfadiazine therapy was instituted, and the patient also received several administrations of typhoid vaccine. This treatment was temporarily discontinued when she had what appeared to be a subarachnoid hemorrhage. During this therapy, there was great clinical improvement; in November, however, her chills, fever and night sweats recurred, and blood cultures were again positive. Sulfadiazine therapy was reinstituted, with clinical improvement again. One important point brought out in the discussion of this case was that crude liver extract or crude preparations of the vitamin B complex should not be administered when the sulfonamides are being employed; apparently the *p*-aminobenzoic acid responsible for the inactivation of these drugs is present only in the crude forms.

The speaker of the evening was Dr. Henry A. Christian, whose subject was "Glomerular Lesions of Subacute *Streptococcus Viridans* Endocarditis." This study was based on 61 patients at the Peter Bent Brigham Hospital with this disease. The gross descriptions were taken from the records, whereas the microscopic descriptions and conclusions were those of the speaker. It was interesting that in the gross these kidneys revealed the typical flea-bitten appearance in only 13 per cent of cases. A moderate amount of edema and swelling was a common finding, on the other hand. Ninety per cent of the organs had infarcts microscopically, and 25 per cent of these were not noted grossly. It was concluded, therefore, that this already high percentage might have been even higher if better sections had been chosen. A correlation with the clinical record revealed that such infarcts are entirely unpredictable, for they seem, of themselves, to cause no urinary signs and symptoms.

Microscopically, the changes in the tubules are neither striking nor specific nor primary. The changes in the glomeruli, however, are multiple, somewhat specific and important. In 80 per cent of the specimens, there was an intracapsular proliferation of cells, which were mostly endothelial but, to some extent, epithelial. This lesion, which is essentially the same as that of diffuse glomerulonephritis, appears to have little if any effect on the measurable kidney functions and causes no appreciable change in the urinary output or sediment. Some of these cells undergo varying degrees of degeneration, with a tendency for granularity of the cells and a decrease in size of the nucleus. Locally, epithelial crescents are found in 36 per cent, with fibrous degeneration of the cells in 26 per cent of specimens. The fibrous crescents may be detached from Bowman's capsule — an indication that degeneration occurs in the fibrous stage. Completely disorganized glomeruli are occasionally found, are variable in any given patient, and interestingly enough, are not found in those with the worst kidney function. Embolic lesions are fairly frequent, but there are few in any given section. They are present in about 40 per cent of the kidneys, but were numerous in only 4 cases. Masses of *Strep. viridans* organisms are present in approximately 6 per cent of cases. The most frequently encountered lesions macroscopically and microscopically are, respectively, infarcts (90 per cent) and a diffuse cellular proliferation similar to that of glomerular nephritis (85 per cent). Dr. Christian believes that the hyaline changes are a manifestation of embolic thrombotic lesions, which are not found in normal glomeruli, contrary to the teaching of some.

Clinically, albuminuria appeared in about 75 per cent of cases, although the same degree of infarction was present in the remainder; hence, infarction cannot be the sole cause of this sign. Casts were found in surprisingly few urinary sediments and were usually of the simple variety. Hematuria was also present in 75 per cent of patients, but was rarely persistent. There were usually recurrent attacks of microscopic hematuria.

Correlation of the clinical and pathological findings reveals that infarcts are not a significant factor, and that embolic thrombotic lesions are not often associated with hematuria. Probably, the most constant association is with focal lesions, especially those of the epithelial crescent type. On the whole, the kidney function remains surprisingly good to the end. In no case in Dr. Christian's series did death result from uremia. The phenolsulfonphthalein and urea-clearance tests were usually good, and it was found that infarcts might involve a large portion of the kidney without significantly impairing the function during the life of the patient.

The discussion was opened by Dr. James P. O'Hare, who emphasized certain facts brought out by Dr. Christian and raised the question of why there is no elevation of blood pressure in this condition, as in chronic glomerulonephritis. Dr. Laurence B. Ellis, of the Boston City Hospital, in corroborating the rarity of terminal renal manifestations, observed that he had seen only one such case in over five years of observation.

In closing the discussion, Dr. Christian stated that the probable reason for the lack of hypertension is the absence of true vascular lesions. The lack of urinary symptoms is probably due to the short course of the disease. Nevertheless, lesions have been found in experimental poisoning with uranium, so that they may be considered nonspecific glomerular lesions. And since the lesions found in glomerulonephritis are the same as those caused by the *Strep. viridans*, it is possible that the lesions of the former condition are the result of the streptococcus itself rather than an effect of allergy, which is the most widely accepted current belief.

BOOK REVIEWS

Malignant Disease and Its Treatment by Radium. By Stanford Cade, F.R.C.S. 4°, cloth, 1280 pp., with 623 illustrations, many in color. Baltimore: William and Wilkins Company, 1940. $18.00.

This elaborate study, which gives a comprehensive picture of treatment by radium of cancer, is praiseworthy but outmoded. The swift progress in roentgen-ray therapy has so altered the field that as one leafs through these pages one is reminded of the brave but tactically outmoded struggles of the British and French armies against the Panzer divisions. The photographs of wooden helmets for the application of radium to an intracranial tumor, for example, have more value as a medical curiosity than as an aid to the tumor therapist.

The section on the physical aspects of radium is adequate, and the section on the biologic effects of radiation is interesting, although somewhat sketchy. The illustra-

tions are clear and well chosen. Some of them are in color.

For the experienced practitioner who has a wide knowledge of the uses and limitations of radium and x-ray therapy in the field of cancer, the book will be of value. For others, although well and honestly written, it cannot but be misleading.

Bibliographia Primatologica: A classified bibliography of primates other than man. Part 1. *Anatomy, embryology and quantitative morphology; physiology, pharmacology and psychobiology; primate phylogeny and miscellanea.* By Theodore C. Ruch, B.Sc., Ph.D. With an introduction by John F. Fulton, M.D., Ph.D. 4°, cloth, 241 pp. Springfield, Illinois: Charles C Thomas, 1941. $8.50.

The use of primates as experimental animals, particularly in the study of the intricacies of the brain, in recent years has resulted in many studies on the animals themselves. Laboratories of primate biology have come into being, bringing new knowledge of the habitats, conditions favorable to transportation, details of sexual life and conditions of breeding. Some types, of great research value, are now being bred for the first time in this country.

With this impetus to study of the primates, the literature, scattered widely in many journals, needed correlation and classification. This Dr. Ruch has done, with bibliographic accuracy, for nearly four thousand separate articles. To the usual reference material are added many facts in abbreviated form: the proportion of the paper given to primate material when other topics are considered; notes on plates, figures, tables and references; and the genera of the animals studied.

This painstaking and finely done piece of bibliographic research is the first book issued under the auspices of the Historical Library of the Yale Medical Library. It augurs well for future publications from this source.

Leaders of Medicine: Biographical sketches of outstanding American and European physicians. By Solomon R. Kagan, M.D. 8°, cloth, 176 pp., with 4 illustrations. Boston, Massachusetts: The Medico-Historical Press, 1941. $3.00.

This volume is in the familiar pattern of Dr. James J. Walsh's *Makers of Modern Medicine*. It consists of a dozen brief biographic sketches of outstanding American and European physicians of the nineteenth century, from Jacob Henle to William Henry Welch. There are engraved portraits of both these men, and of Paul Ehrlich and Jacob Solis-Cohen.

All the biographies are extremely vivid and well documented. The best is that of Sir William Osler, perhaps because he was intrinsically the greatest of the group. Others of almost equal interest, however, are those of Virchow, Mitchell, Jacobi, Allbutt, Billings, Cohnheim and Weigert.

A great debt of gratitude and appreciation is owed to Dr. Kagan as a continuator of the work of Walsh and of Garrison as American medical historians.

Essentials of Electrocardiography: For the student and practitioner of medicine. By Richard Ashman, Ph.D., and Edgar Hull, M.D. Second edition. 8°, cloth, 373 pp., with 122 illustrations and 5 tables. New York: The Macmillan Company, 1941. $5.00.

The second edition of this valuable text will be greeted with interest by all who are familiar with the first. They will find practically a new book incorporating a great deal of material regarding the basic theory of the electrocardiogram that has come to light within the last five years. They will also find a much more adequate treatment of the subject of chest leads than was possible in the first edition.

Unlike many textbooks, this volume is stimulating reading because it bears the stamp of originality all the way through and is not merely a summary of the work of others. Although some students of the subject will find points of disagreement, the general presentation leaves little to be desired. To this reviewer, however, it appears that the authors have, on the basis of theory, carried their refinement of electrocardiographic diagnosis a little farther than existing post-mortem correlations warrant. Specifically, one could wish for a more substantial basis than the authors present for interpretation of deviation of the axis of the T waves in clinical terms. Because of the already prevailing tendency of physicians to read too much into the electrocardiogram, this book is to be recommended more to cardiologists of experience than to beginners.

Essentials of Dermatology. By Norman Tobias, M.D. 12°, cloth, 497 pp., with 143 illustrations. Philadelphia: J. B. Lippincott Company, 1941. $4.75.

The reviewer was amazed at the dermatology contained in this small book, free from the usual verbiage of most textbooks on dermatology. The clinical descriptions are concise, the histopathology contains the necessary details, and the treatment is practical. The classification of the diseases is not confusing, owing to the repetition of entities overlapping in the various sections, when the disease cannot be classified in any one group. The book reflects the author's comprehensive knowledge of the literature, for otherwise he would not have been able to insert essential principles of past and present dermatology. It is noticeable that the little volume includes the most recent studies in dermatology.

The author deals with the treatment of cutaneous diseases in a most practical manner. The prescriptions suggested are not of the shotgun variety, but are sensible in their simplicity, with explanations of the reasons for their use.

The book is legibly printed on good paper, compact and well illustrated. Many of the pictures are excellent; however, at least a third of them, because of poor photography, could be removed without loss. This book is so easily read that it would be no task to the student, and therefore can be recommended to him. It would be very useful to general practitioners and even to dermatologists who desire a quick review of the essentials in their specialty.

Microbes Which Help or Destroy Us. By Paul W. Allen, Ph.D., D. Frank Holtman, Ph.D., and Louise Allen McBee, M.S. 8°, cloth, 540 pp., with 102 illustrations and 13 color plates. St. Louis: The C. V. Mosby Company, 1941. $3.50.

This semipopular account of bacteriology covers the entire field, with emphasis on history, public health and the prevention of disease. The story has been told in better form many times before, and it is difficult for the reviewer to see why this book was published. Many of the illustrations are poor and crude. The facts in general are correct, and the book may be safely put in the hands of the public. As a text of particular value, however, it cannot be highly recommended.